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ABSTRACT

A research workshop was organized to bring together geneticists, psychologists, and other behavioral scientists. The intent was to bring about an interaction of ideas concerned with the genetics of behavior and learning. The emphasis was upon interdisciplinary study among scientists from several fields. Specific issues were isolated in those areas where the research of one scientist was applicable to the questions of another. The workshop format consisted of the presentation of prepared papers and informal discussions among twenty invited participants. Among the topics discussed were heritability, frequency-dependent genetically-controlled behavior, inheritance of somatotypes, methods of I.Q. measurement, and the use of cooperative studies in the collection of core data. No specific workshop conclusions were reached, since the intent was the stimulation and facilitation of interdisciplinary interactions. Post-workshop communication among the participants indicates that some long range benefits will be realized. The program was sponsored by the National Academy of Sciences and the National Academy of Education. It was supported by the U.S. Office of Education. (BW)

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COBRE Research Workshop
on
GENETIC ENDOWMENT AND ENVIRONMENT IN THE DETERMINATION OF BEHAVIOR

October 3-8, 1971
Rye, New York

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THE DETERMINATION OF BEHAVIOR
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WORKSHOP REPORT "GENETIC ENDOWMENT AND ENVIRONMENT IN THE DETERMINATION OF BEHAVIOR" by Lee Ehrman

1. "Gene-Environment Interactions and the Variability of Behavior" by L. Erlenmeyer-Kimling

2. "Quantitative Aspects of Genetics and Environment in the Determination of Behavior" by J. C. DeFries

3. "Human Behavioral Adaptations - Speculations on Their Genesis" by I. I. Gottesman and L. L. Heston

4. "Genetic Determination of Behavior (animal)" by Gerald E. McClearn

5. "Human Behavioral Genetics" by N. E. Morton

6. "Biochemical Genetics and the Evolution of Human Behavior" by Gilbert S. Omenn and Arno G. Motulsky

7. "Genetic Determination of Behavior (mice and men)" by P. A. Parsons

8. "Qualitative Aspects of Genetics and Environment in the Determination of Behavior" by Claudine Petit

9. "The Meaning of Cryptohomunculus" by Ethel Tobach

10. "The Future of Human Behavior Genetics" by S. G. Vandenberg

CG 007 167

WORKSHOP REPORT

GENETIC ENDOWMENT AND ENVIRONMENT IN THE DETERMINATION OF BEHAVIOR

Wainwright House, Rye, New York,
and the
State University of New York, Purchase, New York
October 3-8, 1971

Sponsored by the
Committee on Basic Research in Education
Division of Behavioral Sciences
National Academy of Sciences
National Research Council
National Academy of Education

Workshop Director: Dr. Ernst Caspari
Workshop Coordinator: Dr. Lee Ehrman

Prepared by Dr. Lee Ehrman, Workshop Coordinator
Division of Natural Sciences
State University of New York
Purchase, New York 10577

The Coordinator takes this opportunity to state her conviction of the value and the timeliness of such a workshop topic. Indeed, for anyone involved in anyway in the science of genetics, such efforts as coordination required were gladly offered so that this meeting could take place. The coordinator wishes to thank Drs. Sherman Ross and Barbara Meeker (and Mrs. S. Jobst) for both instructive and constructive assistance.

One almost regrets the completion of this report because of the friendships this entire project engendered over a period of more than a year.

Lee Ehrman

Lee Ehrman, Ph.D.

Background: Participants and Procedures

From Sunday, October 3, 1971 through Friday, October 8, at Wainwright House (260 Stuyvesant Avenue, Rye, N. Y. 10580), with the State University of New York, College at Purchase, Purchase, New York 10577, as hosts, a workshop was held on Genetic Endowment and Environment in the Determination of Behavior. The Chairman of this workshop was Professor Ernst Caspari, with Professor Lee Ehrman serving as Coordinator. Mr. John Hewitt managed facilities and services at Wainwright House.

The following is the description of the proposed workshop as it was circulated with the invitations to attend.

4.

A Brief Description of the Scope of the Research Workshop:

Genetic Endowment and Environment in the Determination of Behavior

A research workshop on the genetics of behavior and learning cuts across many disciplines. At the very least, those of animal behavior, anthropology, biochemical genetics, cytogenetics, demography, ecology, ethology, evolution, population genetics, psychiatry, psychology, and sociology are intimately involved -- this is not to omit the new interdisciplinary field of behavior genetics itself. This hybrid subject has recently been graced with its own journal, Behavior Genetics. Its editors (Professors S. Vandenberg and J. DeFries of the University of Colorado) found it necessary to state the following in their introductory address: "It is most clear from recent events that the misunderstandings inherent in the old nature-nurture controversy are not dead and buried, but alive and well. In fact, this topic seems to generate today as much emotional reaction with as little information as in the past. Perhaps when appreciation of the substantive and methodological informations of behavior genetics becomes more widespread, people will be able to cope more effectively with such issues."

So it would seem wise to make the theme of our workshop, Genetic Endowment and Enviornment in the Determination of Behavior (see E. Caspari, American Educational Research Journal, 5:43-55. January, 1968).

Our reason for planning this workshop is the recognition that 1) the question of the relationships between genetic characteristics and behavior is an interesting scientific question and an important one for understanding human behavior and learning, and 2) that this problem has been approached in different ways by geneticists and psychologists. There are important problems within each science. For example, both geneticists, psychologists and other scientists face the problem of conceptualizing, measuring, and manipulating the phenomena they study. Some of the problems within these sciences, as well as questions, which are frequently ignored by a given science, could be usefully approached by the application of expertise from alternate fields. Behavioral scientists are often ignorant of each others research, or unable to interpret the findings of research because of a lack of familiarity with the methods, theories, and accomplishments of other approaches to research into behavior.

Our intention is to bring together geneticists, psychologists, and other behavioral scientists, whose previous work is directly relevant to these problems, to interact with each other, and to learn from each other. We expect that discussion will try to isolate issues in these areas where the research of one science is applicable to the questions of another, and areas in which research using any approach or combination of approaches has not yet been done but could or should be.

In format, the workshop will consist of discussion of papers prepared and circulated in advance by some of the participants, as well as more informal discussion. We plan to invite about 20 participants, and to meet for one week, in October 1971, at a suitable location. In this way, researchers and students in this broad field(s) encompassing both the biological and social sciences, can benefit from communicating freely with one another for a few days and perhaps an easily accessible permanent report of the proceedings may be complied.

The following is a sample of a letter of invitation to a consultant, i.e., "paper preparer."

7.

January 18, 1971

Dr. Irving I. Gottesman
Department of Psychology
University of Minnesota
Minneapolis, Minnisota 55455

Dear Dr. Gottesman:

Ernst Caspari and I are organizing a five day workshop on Genetic Endowment and Environment in the Determination of Behavior (please see enclosed description). This will be held at Wainwright House in Rye (Westchester County), New York, from October 3-8, 1971.

The workshop is being carried out under the auspices of the Committee on Basic Research in Education, which is sponsored jointly by the National Academy of Sciences and the National Academy of Education. The program is supported by the U.S. Office of Education and the effort is administered by the Division of Behavioral Sciences of the National Research Council-National Academy of Sciences.

The Committee is prepared to cover your traveling and living expenses for the duration of the workshop in addition to a fee of $500 for the preparation of a paper in advance. We ask that your paper involve the relationship between behavior and evolution, as you see fit to interpret this topic; this paper will then be replicated and sent to all workshop participants. It will not be read by you and will be discussed, instead, by another participant and a general discussion will follow.

Since we are sure that your paper will be an excellent one, we sincerely hope that you find our proposal agreeable and acceptable. Please let me know your thought on this matter soon. We will keep you informed of additional details and once I hear from you, a formal letter from Washington will follow.

Most Respectfully,

Dr. Lee Ehrman
Workshop Coordinator

The following is a sample of the letter of invitation to a discussant:

January 18, 1971

Dr. William Thompson
Psychology
Queens University
Kingston, Ontario
Canada, N.W. 1

Dear Dr. Thompson:

Ernst Caspari and I are organizing a five day workshop on Genetic Endowment and Environment in the Determination of Behavior (please see enclosed description). This will be held at Wainwright House in Rye (Westchester County), New York, from October 3-8, 1971.

The workshop is being carried out under the auspices of the Committee on Basic Research in Education, which is sponsored jointly by the National Academy of Sciences and the National Academy of Education. The program is supported by the U.S. Office of Education and the effort is administered by the Division of Behavioral Sciences of the National Research Council-National Academy of Sciences.

The Committee is prepared to cover your traveling and living expenses for the duration of the workshop, so that you may participate as the discussant of a paper on gene-environment interaction in determining behavior prepared, and delivered to you in advance, by Dr. Erlenmeyer-Kimling, who will not read her own paper. A general discussion will follow.

Since we are sure that your discussion will be an excellent one, we sincerely hope that you find our proposal agreeable and acceptable. Please let me know your thoughts on this matter soon. We will keep you informed of additional details, and once I hear from you, a formal letter from Washington will follow.

Most respectfully,

Dr. Lee Ehrman

LE:kg

The following who were invited to participate could not attend:

Professor E. Spiess, University of Illinois
Professor J. Hirsch, University of Illinois
Professor D. Hamburg, Stanford University
Professor A. Motulsky, University of Washington (co-author of a paper)

Those who did not participate were:

PARTICIPANTS

RESEARCH WORKSHOP

ON

GENETIC ENDOWMENT AND ENVIRONMENT IN THE DETERMINATION OF BEHAVIOR

October 3-8, 1971

Wainwright House
Rye, New York

CONSULTANTS

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New York, New York 10032

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Boulder, Colorado 80302

I. I. Gottesman
Coordinator of Research and Training
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University of Minnesota
Minneapolis, Minnesota 55455

Gerald E. McClearn, Director
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Boulder, Colorado 80302

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Population Genetics Laboratory
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Honolulu, Hawaii 96822

Arno Motulsky & G. Omenn
School of Medicine
University of Washington
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Ethel Tobach
Department of Animal Behavior
American Museum of Natural History
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Steven G. Vandenberg
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DISCUSSANTS

V. Elving Anderson
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John L. Fuller
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Binghamton, New York 13901

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Department of Biobehavioral Sciences
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Storrs, Connecticut 06268

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University of Iowa
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Arthur R. Jensen
Institute for Human Learning
University of California
Berkeley, California 94720

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Department of Anatomy and Anthropology
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Chapel Hill, North Carolina 27514

S. Prakash
Department of Biology
University of Rochester
Rochester, New York 14627

W. R. Thompson
Professor and Chairman
Department of Psychology
Queens University
Kingston, Ontario, Canada

Peter Workman
Department of Anthropology
University of Massachusetts
Amherst, Massachusetts 01002

OTHER

Ernst W. Caspari, Workshop Director
Department of Biology
University of Rochester
Rochester, New York 14627

Henry David
Executive Secretary
Division of Behavioral Sciences
National Academy of Sciences-
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Washington, D. C. 20418

Theodosius Dobzhansky
c/o Professor P. Allard
Department of Genetics
University of California
Davis, California 95616

Bruce K. Eckland
Department of Sociology
University of North Carolina
Chapel Hill, North Carolina 27514

Lee Ehrman, Workshop Coordinator
Division of Natural Sciences
SUNY College at Purchase
Purchase, New York 10577

Laurence Goebel
Basic Research Branch
Division of Research
National Center for Educational
Research and Development
U. S. Office of Education
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President
The Spencer Foundation
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Chicago, Illinois 60611

Susi Koref-Santibanez
Rockefeller University
New York, New York 10021

Barbara F. Meeker
Staff Associate
Committee on Basic Research in Education
Division of Behavioral Sciences
National Research Council
Washington, D. C. 20418

Sherman Ross
Executive Secretary
Committee on Basic Research in Education
Division of Behavioral Sciences
National Research Council
Washington, D. C. 20418

The following is the final schedule for this workshop; note that neither the chairman nor the coordinator wrote or formally discussed papers:

WORKSHOP ON GENETIC ENDOWMENT AND ENVIRONMENT IN THE DETERMINATION OF BEHAVIOR

OCTOBER 3-8, 1971

Ernst Caspari - Director
Lee Ehrman - Coordinator

Day	Topic	Consultant	Discussant
Day I	Quantitative aspects of genetics and environment in the determination of behavior	J. DeFries	J. Fuller
	Qualitative aspects of genetics and environment in the determination of behavior	C. Petit	A. Manning
Day II	Genetic determination of behavior (animal)	G. McClearn	S. Prakash
	Genetic determination of behavior (human)	P. Parsons	L. Heston
Day III	Relationship between behavior and evolution	I. Gottesman	W. Pollitzer
		Motulsky & Omenn	E. Anderson
Day IV	Gene-environment interaction in determining behavior	L. Erlenmeyer-Kimling	W. Thompson
		E. Tobach	A. Jensen
Day V	Methodology in the analysis of human behavior genetics	N. Morton	P. Workman
		S. Vandenberg	B. Ginsburg

15.

State University of New York

College at Purchase
Purchase, New York 10577

Office of the President

September 27, 1971

To: Vice Presidents, Deans, and members of the Letters
and Science Faculty:

During the week of October 4, The National Academy of Sciences is sponsoring a Workshop on Genetic Endowment and Environment in the Determination of Behavior. While the working sessions will be held at Wainwright House in Rye, the College is the host institution for this distinguished international study group. Dr. Lee Ehrman was asked by the Academy to coordinate the Workshop, and can give you any specific information you might desire.

You are cordially invited to attend a reception for the distinguished guests on Monday, October 4th, from 5:00 to 7:00 p.m. in the Administration Building.

Abbott Kaplan

Abbott Kaplan

Telephone: (914) 253-5000

CONCERT PRESENTED IN HONOR OF AND
ATTENDED BY PARTICIPANTS IN THE WORKSHOP

JEAN AND KENNETH WENTWORTH

in a program of original works
for one piano, four hands

Purchase October 7, 1971

Sonata in B flat, K. 358 Allegro Adagio Molto presto	Mozart
Variations on a National Air of Moore (1826)	Chopin
Concerto for Piano Four Hands & Tape (1969) (Written for Jean and Kenneth Wentworth)	Wm. Sydeman
INTERMISSION	
Fantasy in F minor, Opus 103	Schubert
LaGallina Grand Tarantelle, Opus 67	L. M. Gottschalk

* * * * * * * * * * *

JEAN and KENNETH WENTWORTH, both graduates of the Juilliard School where they were scholarship students in the class of Irwin Freundlich, have specialized in music for four hands at one piano. Jean Wentworth, a winner of the coveted Walter W. Naumburg Award in 1954, has appeared extensively as piano soloist. Since their first concerts in 1964 in India and the Middle East sponsored by the United States Information Service, the Wentworths have been heard in New York (including a feature Channel 13 TV appearance), Boston, Philadelphia, Washington, London, Vienna, Brussels, Madrid and Rome. In addition to exploring the much-loved traditional repertoire, the couple have also commissioned and performed many new works. The contemporary works on this program were written for the Wentworths.

October 11, 1971

Mr. John Hewitt, Manager
Wainwright House
260 Stuyvesant Avenue
Rye, New York 10580

Dear Mr. Hewitt:

This is to thank you for the splendid job and special efforts you managed for the National Research Council-National Academy of Education Workshop recently held at Wainwright House. As representative of the host institution, The State University of New York, College at Purchase, let me call particular attention to your gracious staff, superb food (your chef well deserved the special round of applause, etc, accorded him), and your own helpful patience with me.

I personally hope we have an opportunity to collaborate again soon, in the cause of scientific advancement and in the pleasantness of Wainwright House.

Most respectfully,

Lee Ehrman, Workshop Coordinator
and Associate Professor of Biology.

LE/fbf

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To: All Participants in the Workshop on Genetics Endowment and Environment in the Determination of Behavior.

From: Lee Ehrman, Division of Natural Sciences, State University of New York, Purchase, New York 10577.

Re: Pertinent Remarks Made During the Discussions at Wainwright House, etc.

Would you please consider sending to me, soon and in typewritten form, notes about any remarks made during the general discussions which you want to call to the editors' attention? These need not be exchanges in which you yourself participated.

Discussants are requested, in addition to the above, to compile brief summaries of their presentations. (5-10 double-spaced typewritten pages).

Revised (not lengthened) versions of consultants' formal papers are due by November fifteenth.

Second copies of all items should be mailed to the co-editor:

Dr. G. Omenn
School of Medicine
University of Washington
Seattle, Washington 98105

THE WORKSHOP PAPERS

1. De Fries wrote on "Quantitative Aspects of Genetics and Environment in the Determination of Behavior." His fine paper, as discussed by Fuller, elicited an ongoing debate about the proper way to define heritability -- this debate still not having been terminated by the end of the five-day long workshop! De Fries cautioned against the difference and the confusion between heritability in the narrow (ratio of additive genetic variance to phenotypic variance) and in the broad (proportion of phenotypic variance due to both additive and nonadditive genetic variance) senses. Heritability in the narrow sense is the one which should concern genetic counselors. He then proposed a new coefficient of environmental determination, r. It is defined as the proportion of the total variance for some population character, e.g., intelligence, which is due to measured environmental effects. r has both descriptive and predictive values since it may serve as an index of the value of the environment in which an individual developed as well as an indicator of the effects of controlling environmental variance in a population. No valid estimate of r is currently available.

Other than the above, the general discussion of this paper concerned:

a) the value of r for intelligence, presumably high;

b) the effects of assortative mating, not kinship;

c) the fact that, to a certain extent, an organism may choose its own environment though parents select their children's habitat;

d) results of dog-coyote crosses;

e) spatial discrimination in Eskimo-Aleut crosses;

f) endocrine domestication in our farm animals;

g) correlation and covariance in genetic-environment interaction and the fact that sometimes different genotypes have different environments associated with them;

h) the not entirely frivolous question of whether or not circumcision is hereditary; and

i) is man a wild species (or a weed species -- surely he is not a garbage species)? The key point here is that a domestic species has its reproduction regulated by man whereas man does not officially regulate his own reproduction.

2. Petit's paper, the dizygotic twin of De Fries', concerned "Qualitative Aspects of Genetics and Environment in the Determination of Behavior." In it a very wide survey of the literature was undertaken -- wide in view of the variety of organisms discussed (insects, mice, cats, guinea pigs, man, etcetera), and wide because of the phenomena considered (from single gene effects on behavior through imprinting). But surely, Petit's primary and unique point, one that occupied most of Manning's discussion, was her own data on frequency-dependent genetically-controlled behavior. This is known to occur in Drosophila males, and elsewhere, as an advantage in the acquisition of mates by rare males. It can be recorded by either direct observation of the matings or via the scoring of the progeny of rare males. And once these rare males become less rare in their respective populations because of their sexual advantages, they lose this advantage. Finally, an equilibrium is achieved.

Other than the above some of the general discussion concerned:

a) the fact that yield in a given area improves if a mixture of seeds, not one kind, are planted there;

b) the beautiful work of Rothenbuhler on single gene units and units of behavior in bees;

c) Kummer's observations on baboon troops, especially the hamadryas one-male units;

d) Kojima's work on frequency-dependency with regard to the esterase locus in Drosophila;

e) the genetics of song in acoustical insects such as crickets;

f) most important, the definition of culture. This final point was pursued at length for a couple of days, and two offered definitions stand out. Culture is the sum of learned behaviors. Culture is the imposition of arbitrary form on the environment. (Arbitrary in the sense that it can be changed in a single generation). In view of these definitions, is there such a thing as subhuman culture?

3. McClearn addressed himself to the "Genetic Determination of Behavior (Animal)." He reviewed the comparative method as applied to behavior genetics, i.e., what can we learn about the genetics of learning from experiments conducted with mice and with rats? And his final point, a warning against the generalizability of results obtained with genetically unspecified animal subjects is worth quoting in its entirety:

> Replicability, that sine qua non of a science, suffers when research is conducted on the nondescript groups used by so many contemporary researchers, and thus the cumulative build up of knowledge that is supposed to characterize a science is severely impaired. The use of genes as variables, to be held constant by choice of a single strain for investigation; to be manipulated as fixed effects by making strain comparisons; to be manipulated by selective breeding; or to "randomize" by use of a deliberately genetically heterogeneous stock, can increase research efficiency greatly.

In the discussion of this paper, led by Prakash, McClearn outlined the history of behavior genetics as we know it today. He told of the first mazes, Heron's and Tryon's and of the student, Skinner. Watson's famous quote (originally appearing in the Proceedings of the Royal Society, Section B) was read by Tobach. This paralleled the opening remarks by Chairman Caspari, citing the seminal works of

B.S. Burks, The relative influence of nature and nurture upon mental development, Yearbook of the National Society for the Study of Education, 1928, 27: 219-321;

and

R.C. Tryon, Genetic differences in maze-learning ability in rats, Yearbook of the National Society for the Study of Education, 1940, 39: 111-119;

and the oft-quoted collection of

J. Hirsch (Editor), Behavior Genetic Analysis, 1967, McGraw Hill, New York.

4. Parsons considered the "Genetic Determination of Behavior (Mice and Men)"--thus continuing the approach taken by McClearn. He was, however, particularly concerned with an estimation of genotype X environment interactions and with the isolation of their component parts. With this goal in mind, Parson has studied three strains of mice differing in genotype weight, skeletal morphology, and in behavior in a consistent relationship to one another. His results support postulated associations with somatotypes (Sheldon) and behavior in man. These include criminality with mesomorphy, schizophrenia with ectomorphy, paranoia with mesomorphy, ectomorphy with slow physical maturation in women, etc. So Parsons recommends that associations between morphology and behavior in man be investigated more thoroughly. Then he offered feral mice (once but no longer commensal with man) and aboriginal mice (never associated with man), as well as commensal mice for consideration as desirable experimental subjects.

Heston's discussion of this paper led to spirited exchanges when he boldly inquired, "Isn't our interest, no matter what our experimental animal, really human behavior?" And other than certain studies of audiogenic seizures, Dr. Heston deemed obsession with inbred strains and much other experimental work in behavior genetics irrelevant to the human condition. As a clinical psychiatrist he pleaded for more assistance from those who experiment with animals and bemoaned the lack of help animal models have provided so far. The general discussion brought out:

a) a comparison between the self-mutilation evinced in the

Lesch-Nyhan syndrome and behavior such as the eating of young observed in captive animals;

b) how little is known about the inheritance of somatotypes;

c) the relationship between gout and achievement; e.g., gout and the number of publications of university professors;

d) the more than one hundred neurological mutants known in mice;

e) phenotype X phenotype interaction, such as the sorts of gifts certain somatotypes receive at Christmas, e.g., the ectomorph gets a book, the mesomorph, boxing gloves, and the endomorph, candy;

f) the fact that we should consider, besides genotype X environment interactions, genotype X genotype, phenotype X phenotype, and phenotype X environment interactions.

Heston vigorously suggested that those of us who wish to elucidate the role heredity plays in the determination of behavior, "get down to proteins." This led nicely into the Omenn-Motulsky paper the next day.

5. Gottesman and Heston wrote on "Human Behavioral Adaptations-Speculations on Their Genesis." And they did so superbly. To comment further on only one of their points, they recorded what is known about the evolution of milk drinking. Human populations differ in the concentrations they are able to produce of the enzyme lactase. In its absence, ingested lactose simply passes through the alimentary canal without serving as an energy source, a food, and in doing so, causes cramps and diarrhea. This enzyme deficiency is now known to be genetically controlled though not simply (i.e.,more than one set of alleles is involved). European populations can employ milk as food; Asian, Amerindian, and African populations are generally lactose intolerant. Implications for pediatric advice and for school lunch programs, etcetera, are obvious: Not everyone needs milk! To give it to some individuals is to do harm.

It appears that primitive man like other animals was lactose intolerant after infancy and that the ability to cope with this sugar must have evolved. "We may then ask what magnitude of selective advantage would have been required to change the frequency of a favorable dominant mutation to currently observed levels" (90-100% tolerant in northern Europe, 0-10% elsewhere). Pollitzer, the discussant-editor of the Journal of Physical Anthropology - distributed copies of a map illustrating traditional areas of milking and nonmilking. It was divided into three categories; nonmilking predominant, milking predominant, and absolutely nonmilking.

The rest of the general discussion dealt with another Gottesman-Heston topic, that of primate phylogeny. The work of Simons and Pilbeam, both of Yale University, on Ramapithecus and his reduced canines, was mentioned. Mosaic, cladogenetic, anagenetic, and phylogenetic evolution were noted, as was the contribution of Fitch and Margoliash. An amusing point was the statement that despite repeated and ingenious attempts, chimpanzees fail to speak not so much because they lack a suitable vocal chords, but because they have nothing to say. Finally, Thiessen's notion of "genetic junk" was defined and redefined. Apparently genetic junk includes traits with very high heritability.

correction
7

6. Omenn addressed himself to "Biochemical Genetics and the Evolution of Human Behavior." Following a general introduction, the evolutionary development of the biological substrate was reviewed -- the substrate being proteinaceous material. Then the evolution of allelic gene products, mutation in the narrow sense, and evolution by gene duplication were discussed. At this point, the

Omenn-Motulsky paper was shifted in its tracks in order to concentrate upon the human nervous system. The human brain was approached in a number of ways, none more fruitfully -- for the purposes of this workshop -- than from the points of view of protein polymorphisms and enzyme variation within tissues of this unique organ. This most extensive and exhaustive paper concludes with a consideration of the central role of language in the evolution of *Homo sapiens*. It is probably beyond the scope of a workshop report like this one, to condense the meat of a paper as long and scholarly, though as fragmented, as Omenn's. So perhaps a survey of the discussion it provoked would be more profitable. This discussion was lead by Anderson who pointed out that Omenn, besides his M.D. degree, would soon be in receipt of a Ph.D. in genetics. Omenn noted his problems concerning the acquisition of specimens of human brain for study. Most of them were bits of surgical specimens although he could perform some enzyme evaluations after death. Then too, his biopsy fragments had to be further divided into glial and neuronal components. Here, comments about matters like the white and gray regions of the frontal cortex and receptors specific for testosterone and estrogen in the brain linked with Pollitzer's discussion of the Gottesman-Heston paper. Pollitzer had previously distributed a table of estimates of "extra neurons" in the brains of Rhesus moneys, baboons, chimpanzees, gorillas - two separate estimates, *Australopithecus africans*, Zinjanthropus, *Homo erectus* - two separate estimates, and *Homo sapiens* "Extra neurons" represent our adaptive capacities; they are not the requisite neurons for housekeeping functions. Neanderthal man might indeed have had a slightly larger (60 or 70-100 cc) brain than modern man - evidence of his degeneration perhaps? The brain of a human female averages 1100-1250 cc these days, while a human male's brain averages 1250-1300 cc. Large brain volumes are not correlated with great intelligence however. Anatole France's brain was relatively small (1100 cc) and Einstein's was average while Jonathan Swift's was relatively large. So, within normal ranges, the relevance of small variations in human cranial capacities is obscure. Omenn noted that in newborn mice brain cells are still dividing for a few days after birth -- a fact not generally realized. In the mouse some fifteen enzyme systems have apparently already been mapped and there apparently are many dozens of known neurological lesions and mutants, among them the pallid gene, also occurring in mink. Pallid alters coat color and causes congenital ataxia as well-- pleiotropy with a vengeance! Omenn offered the McCarthy-Laird-Hoyer work on DNA-DNA and DNA-RNA hybridization for approval. Suffice it to say that it was not a subject not of great interest to the workshop group, and that there is some skepticism about this whole matter. For instance, it occurs to this coordinator that DNA prepared for hybridization tests of all sorts is so abused (specifically denatured), that only a fraction of it ever hybridizes at all during the course of subsequent experiments.

7. Erlenmeyer-Kimling prepared an excellent paper on "Gene Environment Interactions and the Variability of Behavior." Its most useful part is likely to prove a large table on the generality of strain X treatment effects in some early experience studies in mice. These have been separated into:

a) variations in social versus isolation rearing;
b) handling versus nonhandling;
c) infantile trauma - specifically noise;

d) high versus low illumination;
e) enriched versus standard cages;
f) daily drug dosages versus daily saline dosages; and
g) shocks versus treatment devoid of shocks.

Let it be noted now that R. Hernnstein's Atlantic magazine article on different prospective outcomes from different schools depending upon average inputs into these schools was brought up repeatedly, including in the discussion of the Erlenmeyer-Kimling paper. It is entitled "I.Q." (1971, pp. 44-64) and apparently did not win the approval of those workshop participants who had already read it before we met.

Thompson, the discussant, told of his clever work with young rats subjected to physically and therefore mentally restricted biological mothers (during gestation) and enriched rearing mothers later. He also tried the reciprocal combination and found that the order of restriction-enrichment did not influence the outcome, i.e., the capacities, etcetera, of the adult offspring which resulted. From the floor, in several ways, came the suggestion that a single low score in a specific course in school or during a specific school term could mean many things, e.g., a low I.Q., a dislike of the teacher, temporary health conditions, newly arisen conditions of health, etcetera. Then Thompson went on to report on his lick-rate-at-water-spout and electric shock signal experiments in rats (Long-Evans), and of his need to first establish a base line lick rate. Thompson told of a scientist asked the percentage influence of genetics and of environment upon intelligence (that question again!), who replied, "Heredity=100% -- Environment=100%."

A final interesting discussion highlight evoked by Thompson's discussion of the Erlenmeyer-Kimling manuscript was that of handedness;

how is it inherited? Collins' remarkable studies were brought up; they indicate a 1 : 1 proportion of right and lefthanded mice, with no apparent genetic basis for either. I recall the old days when I was taught so sweetly and simply, that righthanded folks were RR or Rr, but certainly R-, that lefthanded ones were rr, and that Rr could be ambidextrous. More seriously, Polansky's study of mental organization and maternal adequacy in rural Appalachia was spotlighted at least twice.

8. Tobach produced a long paper on "The Meaning of Cryptohomunculus." She was to have collaborated on a paper with this title with T.C. Schneirla, to whom this one is dedicated. (He died three years ago.) Cryptomunculus is the little creature, the nymph, thought to be delivered -- every characteristic set -- into its mother's womb, thus continuing parental characteristics from one generation to the next.

There are a number of points in Tobach's paper which require tightening up and I am sure she is aware of this. Her paper was labeled "Final Draft Minus Two - Not To Be Cited." For example, items 2 and 3 on page 3. And I'd like to see her spell out Schneirla's concept of behavioral development (referred to on pages 9 and 17 and elsewhere). But note her pertinent remarks about the Herrnstein article again! For now, aside from a comment about the excellence of the Tobach bibliography, let us pass to Jensen's discussion, the best attended one. He described an I.Q. test or tests he was trying to develop--surely a good idea. We are in desperate need of new and improved methods of I.Q. measurements--methods as "culture-free" as possible. The tests Jensen is fiddling with involve, as a start, reaction time to the illumination of colored lights. Reaction time is a component of athletic ability. He is also considering "bits of behavior," i.e., the ability of children to copy different two and three dimensional shapes (as in the Guttman scale), and the more commonly employed digital span tests. He noted that his tests would allow for repeat and for practice so that reliability of assessment could be checked. And he listed as points of concern:

1. "Relevance"
2. Reliability
3. Heritability
4. Fractionation - an oft-repeated term
5. Genetic Analysis
6. Correlates of Genotypes.

In the general discussion, a comment was made that with a "good I.Q." test, the etiology of serious disabilities would become apparent, i.e., dyslexia and the different types of mental retardation. An individual with a simply low I.Q. would then appear devoid of pathology but younger in mental age. Bias on the part of teachers was repeatedly brought up. How often is a youngster asked, "What does your father do? Morton talked about path coefficients and the question of imput (into school) and output, the latter involving performance variables. Is final output independent of hereditary input or in what way or proportions dependent upon it? Eckland made a very pertinent point in stressing the apparent importance of familial situations in these instances, as recorded in careful surveys he has made. Perhaps good performance in school is in some way positively correlated with docility!

Then the whole group attempted to define race--not a simple task. This problem arose out of Jensen's remarks that performance on I.Q. and other tests by youngsters in Berkeley from different ethnic backgrounds, differed significantly and consistently. My own suggestion that a race is a Mendelian population sharing the same gene pool (and at this point in time, the same evolutionary future), was rejected as pleasing primarily population geneticists. Parson drew up a definition accepted by all. He intends to polish it and it will be incorporated into the published record of these proceedings. Briefly, a race is a population differing from other such populations in gene frequencies; there are no reproductive isolating mechanisms between races. Parsons suggested the possible abandonment of the term race altogether, with population substituting for it. This is a reasonable suggestion, worthy of careful thought.

9. On the final day of the workshop, Morton's paper on "Human Behavioral Genetics" was open for discussion. His stated intent, since his specialty is biometrics, was to consider "the use of mathematics to answer certain biological questions." Point by point, mathematical methods were offered for answering the following questions:

1. What are the effects of single genes on behavior? (See Petit's paper and Manning's discussion of it).
2. What are the effects of chromosomal aberrations on behavior? XO, XXY, XYY, etc. syndromes?
3. How can behavior whose transmission is unknown be screened for sensitivity to genetic differences? Using the Kimling-Jarvik data from a survey of the literature on intelligence tests, Morton shows how he estimates:

0.675	due to genetic differences
0.139	due to environment
0.016	due to common environment (specific for twins)
0.170	environmental miscellaneous
1.000	components of realized intelligence

4. How can the inheritance of behavioral attributes be studied? This, the problem of the entire workshop.
5. Do psychological factors have genetic differences? His correct answer is yes.
6. To what extent are group differences in behavior genetic? There is value in studying group differences

as illuminated by the performance of hybrids between them.

7. What are the effects of behavior on population structure and selection? Here the interesting phenomena collectively called assortative mating are involved. And Morton's final point is that one would suppose that heritability must be low for a trait subject to intense selection, that is, a trait crucial in establishing Darwinian fitness. Such a "trait" would be social dominance.

Workman's discussion involved teacher effects or "Pygmalion in the Classroom", Rosenthal's study. Eckland and others observed that this work could not be replicated. Eckland again stressed the apparent fact that familial factors are the indicators--the only good ones we have--of school performance. Mention was made of the Roberts' study of the social behavior of hemophiliacs--that is, reproductive compensation occurs [illegible] on the part of the siblings of affected individuals, not via affected individuals themselves. This is apparently true of unaffected siblings of hemophiliacs and other afflictions as well. Other points brought out were the deficiencies in assessing the spatial relationship (visual infantilization) observed in Turner's syndrome; Fuller's famous work on the social isolation of young dogs; the high incidence of juvenile diabetes, with mild onset, in South American Indians; the stratification of populations; the fact that migrant workers present material for a mass deprivation experiment; the relationship between stays in orphanages and prostitution which could be misinterpreted as a relationship between religion and prostitution since religious orders often manage orphanages; left and right dermatoglyphic asymmetry and the whole fascinating problem of developmental bilateral asymmetries in general; different heritabilities (again!) in different environments, e.g., alter the temperature for Drosophila and you alter the heritability, etc. Finally, two very important points were raised: 1) What trait does not have a genetic component?

2) The American Negro from the south is likely to have some one percent white ancestry while his northern brother averages 22-25 percent. So, what sort of heterogeneous research material (a "single" population?) does the American Negro represent?

10. "The Future of Human Behavior Genetics" by Vandenberg was our final workshop paper. It was well positioned in the sequence of other papers. In a valuable appendix, Vandenberg offers suggestions for core data which can be collected in cooperative studies. Before this though, he pleaded for more basic theoretical formulations, for instance, about the structure of populations with respect to ability measures. And then he speculates about most likely future research in this new hybrid, behavior genetics.

As discussant, Ginsburg questioned the use of rare diseases as natural models. He opted for the genetic monitoring of sperm donors. And he emphasized the fact that even major genes have different effects on different backgrounds. On all three points, he was absolutely correct. About here, a definition of schizophrenia was requested and even with the assistance of Gottesman and Heston, no satisfactory one was forthcoming. It is apparently a syndrome, somewhat nebulous, in which victims exhibit alternate arrays of a variety of symptoms. Neologisms are not the rule, for example. Ginsburg presented a summary of his own fine studies on audiogenic seizures and on the pharmacogenetics of mice. One dosage of any single drug will not result in the mimicking of a psychosis even in human material--repeated dosages are required. Clinical psychiatrists and clinical psychologists are now observing primarily drug-induced psychoses.

Long Range Workshop Results

At this point with Dr. A. Omenn, a workshop participant, co-editor along with Lee Ehrman, publication of the workshop papers and proceedings is being planned--more than that, is underway. Considering current national and federal concerns, it would be difficult to overestimate the future and present value of this particular workshop. As an example, the participants have already lost no time in communicating with one another again in the short time since the workshop adjourned. Much remains to be done--to be worked out--but for now, it would be premature to state more about the long range benefits. It does seem, however, that some scientific progress will have been realized as a result of this endeavor.

On September 22, a basic course in Genetics for undergraduate upperclassmen was begun (by Lee Ehrman) at SUNY, Purchase. A number of the students enrolled in this course attended sessions of the workshop. They were subsequently asked to evaluate what they heard and read. The following are their comments along with my appended remarks.

CASPARI WORKSHOP

Gregory Coccetti
Genetics
Dr. Lee Ehrman
November 1, 1971

In the past most human behavioral studies have been conducted on infra human animals, such as the white rat and Drosophi~~t~~la, and application of the results have been applied to human behavior. These experiments have been conducted primarily because human experimentation has been difficult and often impossible to perform. However, recent research has made promising advances in the study of human behavior through experimentation on man himself. Equally significant have been advances made in biochemical research and the application of this information to human behavior and genetics. It has been these advancements and the continuing studies conducted on gene-environment interactions and continued infrahuman subject experiments which provide the direction for future studies in behavior genetics.

During many of the discussions taking place at the Caspari Workshop many of these topics were extensively discussed.

For example, Dr. Leonard Heston raised question to the applicability of infrahuman behavioral studies to man. He explained that aside from the genetic information already extracted from previous studies and behavioral patterns which essentially are inherent to these animals, no stimulating information has recently been found. In fact, a new direction in the study of human behavior was necessary. Although a

Psychiatrist's point of view, Geneticists were not discordant instead, Dr. Caspari explained he felt earlier Psychiatrists may have been in error when choosing the white rat as a model for any behavioral studies; except perhaps, for that of the rat itself. Further, Dr. Caspari made a point of explaining that primate studies would probably be more usefull in attempting to study human behavioral patterns. Others remarked, however, that primate studies were both more expensive and more difficult to perform. But Dr. Caspari explained that the closer evolutionary relationship between man and other primates would prove invaluable in behavior studies. And too, primates are more culturally oriented, which provides for an even closer correlation with human behavior.

Dr. Heston also pointed out that another useful tool in attempting to study behavior lies in a better understanding of the biochemical basis of genetics. Or, more work such as presented by Drs. Omenn and Motlusky, in their paper entitled "Biochemical Genetics and the Evolution of Human Behavior", be attempted. Protein analysis and physiological activities, it was mentioned, should be thoroughly investigated and behavior integrated. Dr. Vandenberg in his paper, "The Future of Human Genetics", also echoed that biochemical and physiological research was a promising field for development.

The next topic centered on gene-environment interactions, and their affects on behavior. Dr. Newton Morton proposed a model for his interpretation of environment and intelligence interaction. Here the output phenotype of an individual was correlated to both environmental interaction (eg. educational system) and the genotype of this individual. This is not a new correlation, as Dr. Morton brings out in his paper, "Human Behavioral Genetics," but one which should be reassessed. Dr. L. Erlenmeyer - Kimling's paper, "Gene-environment Interactions and the Variability of Behavior," was completely devoted to gene-environment interactions and their impact on behavior. In his paper, Dr. Kimling expressed a need for more studies in this area for until now "...so little systematic attention has been paid to the implications, extent, and meaningful analysis of interaction."

Lastly and most importantly, a continuation of human studies was urged whenever feasable. Here Geneticists, Sociologists, Psychiatists, and Behaviorists, et al. constantly referenced studies performed on man; yet admittedly the amount of information was decidedly less than that known of other animals.. Naturally, this is an idealist's approach; for the best way to study the behvior of any animal is to experiment with that same animal. However, continued twin studies as performed by Dr. Newton Morton along with studies proposed by Dr. S. Vandenberg in his paper, "The Future of Human Behavior Genetics," which (in) he recommends studies of adopted children, studies of children born to parents married more than once, and others, would provide vital information to such a necessary area of study.

It is certainly difficult to express any particular impression of a conference such as the Caspari Workshop. However, I felt that any information gleaned which would aid the further study of behavior was of significant value both to the participants and myself as a student. Although no conclusion were to be made of the Workshop by inference I believe that the complexities involved with the study of behavior, whether connected with genetics or not, have only increased and have created new problems. It can also be infered that independent studies conducted by various scientists is not the key in diminishing the lack of knowledge in this area. A more prudent, systematic approach in collaboration with other scientists seems in order with more profitable results occuring. Careful consideration of all possible aspects of behavior can only aid in behavioral studies.

ON THE DISCUSSIONS AT THE WAINWRIGHT HOUSE

Amena Ali
Genetics
11-3-71

During the week of October 3, 1971, Dr. Ehrman invited her genetics class (from SUNY at Purchase) to attend discussions concerning genetics at the Wainwright House in Rye, New York. Top scholars in genetics and psychology participated in these discussions.

The ratio of psychologists to geneticists was approximately 1:1. Altogether, about thirty people attended. Out of these thirty people, four were women. The U.S.A., France, India, and England were represented at these meetings.

There were usually two discussions a day. One was from nine in the morning until noon and the other was from two until six, And The time inbetween being for lunch. Sometimes, the second discussion was held later in the afternoon leaving free time. In this free time, tennis games were scheduled and a car was made available for those who wanted to go about the town.

Mostly sporty sweaters and pants were worn to these discussions. This gave an air of informality thus easing the tension of the ever present tape recorder. Jokes were thrown in also to releave the tension, but on the whole the discussions were very informative and enlightening.

Mimeographed copies of the papers to be discussed were made available to the participants well before the discussion period.

At the beginning of a discussion, the proctor and the author of the paper to be discussed would sit in the front-center of the room. The rest of the participants would be arranged to sit in a sort of half moon around the two previously mentioned. The proctor usually presented the paper and views about the paper which would lead into a discussion.

I was unable to fully appreciate the discussions for two basic reasons. Being a junior undergraduate, it was impossible for me to have enough background material in genetics or psychology to be able to intelligently cope with all the material discussed. Secondly, the mimeographed papers for the discussions of the day were made available to me just before the discussions were to take place. This further hindered me from understanding the topic and the problems surrounding that topic.

Behavorial genetics may be said to be that study of heredity and variation of organisms as related to the behavior of the organisms. This type of study is fairly new so that all information obtained on the subject would not be outdated. Behavioral genetics can be a benefit to man but if not used cautiously may become potentially more dangerous than our latest weapons.

If we could relate behavior to the genetic composition of the organisms, so many beneficial advances could be made. The process of learning, with all of its individual differences,

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could be further delved into with a more concrete scientific base. This affects man and mankind alike, and because of this is dangerous if improperly used. "Slow learners" would then be understood. If taken far enough, we would be able to supply enough stimulus to initiate the response of learning. Thus, these individuals would become good learners and a benefit to society.

Imagine, initiating enough stimulus for a given response. The newspapers do it every day. The only difference is that they work on an emotional level where as we would be working on a scientific level. Where the newspapers would sometimes make a mistake in response, we would not.

When we obtain the knowledge to scientifically produce a given response, we will have unimagined power over ourselves. That is why this knowledge and understanding of these experiments must not remain with a select few. When this knowledge is made available to the public, special care must be taken to make sure that all of the facts are told and that the material is not prematurely introduced. You see, non-white people ~~who~~ are directly affected by behavioral genetics AND can be easily victimized by it. One basic reason for this is their lack of knowledge on the subject.

Milk intolerance affects most of the non-white peoples in the world. This is definitely a fact that should be publicized. There are many school programs in this country that serve milk as a part of their lunch program. This should be stopped or continued only if an alternate selection is made available.

One disturbing fact indirectly came out at my visit to the Wainwright House. There was an article published in the New York Times stating that it was scientifically proven that blacks have an IQ lower than whites. Speaking to three of the geneticists about this article, I found out that this scientist had allowed his facts to be misinterpreted. This was not only disturbing but also alarming. Why would a scientist who has worked hard and long on an experiment allow it to be misinterpreted? It is the responsibility of the scientist to see that caution is taken in his material so that it is legible and definite. Withholding facts or any other means of allowing the material to be misinterpreted is not acceptable.

Once a discussion was started at the Wainwright House, it was relatively easy to see who was the geneticist and who was the psychologist. This was shown by the definitions given for natural selection and schizophrenia. Both the geneticists and psychologists were giving definitions inclined to their own trades. Naturally these definitions did not coincide, but it was surprising that no compromise in these definitions could be reached on either of those terms. It may seem a little ridiculous that with the major problems that they are trying to solve, that they have such a problem trying to communicate with each other.

As a result of this, the psychologists seemed to express doubt in where they stand on behavioral genetics. This doubt was unwarrented. There exists a balance of nature and nurture in the world. Nature being the genotype; nurture the surrounding environment or phenotype. The psychologist's job is to examin the phenotype; the geneticist's, to link that phenotype with a genotype. In doing this the psychologist may look at the generality of law, find out what is the basis for the absence of this generality as applied to concrete examples, and the degree of individuality as seen in learning.

In conclusion, I would like to say that it is fine for us to obtain the knowledge needed to make us better understand ourselves but this knowledge must not remain in the hands of a select few. If it does, minorities of peoples may too easily become victimized by this knowledge. More importantly, for now, is the fact that the scholars cannot even talk to each other without one going away doubtful of himself. Better communication should be set up.

GENETIC ENDOWMENT & ENVIRONMENT IN THE DETERMINATION OF BEHAVIOR

Deanna Toone
Dr. Lee Ehrman
Nov. 3, 1971

Deanna Toone
previous student of the Cooperative College in Mt. Vernon, associated with the College at Purchase (SUNY) now attending Junior Year at Purchase.

Having been enrolled as a student~~s~~ of genetics of only one week before attending the meetings at the Wainright House in Rye, New York, my background was somewhat limited, to say the least. The meetings were held the second week of the school semester from 9:00 A.M. to 6:00 P.M. of which I was only able to attend the afternoon sessions because of other academic committments.

For the first two days, I found the meetings to be above my comprehension, and did not earnestly try to indulge in conversation with the scientists ad psychologists. This had nothing to do with the attitudes of the speakers of the meetings, for they were all more than willing to answer any questions we might have wanted to ask.

On the whole, I found both geneticists and psychologists pleasant and receptive to the students.

I felt the meetings gave the scientists a good opportunity to discuss various experiments and concepts with which they were working, in that it might in some way benefit all.

I realized the importance of terminology when the question of race came up. No one could give a definition of "race" which would satisfy everyone: which I feel is essential in science and society. The issue was finally dropped when everyone agreed that "population" would be the preferrable term, because it had a lesser emotional response or reaction than did "race".

One aspect of the meetings which I choose to discuss at this time is the psychological effects of black students when referred to as "negroes". Dr. Heston (I believe) gave a talk on lactose intolerance, in which, he referred to blacks as "negroes"; which to some might seem a trivial matter, but this generations of blacks find the term "negro" both deroggatory and offensive and as a consequence , blacks tend to discount or misinterpret anything a person using the term has said. A good example of this is the fact that all the black students attending this particular session were offended by the term and consequently this seemingly trivial oversite on the part of the speaker; everything he inferred about about blacks was misconstrued by us. Hostility reined through the group of blacks to such a point that we felt compelled to approach the speaker; whereupon he graciously repeated what he had said previously, putting things back into their proper perspective.

The following is a quote from a paper entitled: Human Behavioral Adaptations-Speculations on their Genesis, by Heston and Gottesman concerning lactose intolerance.

"In the case of lactose it appears that a cultural-technological advance, domestication of animals, was inexorably intermeshed with a change in gene frequency. At the same time, the cultural-technological advance must have accelerated the genetic change. The range of cultures and individual behaviors entailed by this genetic-environmental change is obviously extremely broad with ramifications into almost all aspects of life".

In my opinion, the concept of 'cultural-technological' advance' is rooted in anthropological thinking. The linking of the biological concept of an evolving gene pool with a basically anthropological term serves only to associate a biological concept with an idea that has already become associated with some of humanities more regressive thoughts.

In conclusion, I feel compelled to say that modern science generates and is generated by the social structures of its day. Modern science has a two-fold responsibility (1) to achieve the goals of understanding that it sets for itself and (2) a responsibility to the social order in which it strives, which is essential in the study of behavioral genetics.

Problems inherent in the study of behavioral genetics may appear to be similiar, but, sociology and anthropology indicate that they are in fact very different.

Studies within and between Mendelian populations will not ultimately produce the correlations necessary for a basic understanding of behavioral genetics.

Noted by Gottesman and Heston: it is very difficult to distinguish between changes due to behavioral and physiological adaptibility and those due to changes in adaptedness via natural selection leading to gene pool changes. An example of this problem was seen when there was an increased height in Japanese children born to Japanese parents, the USA compared to those born in Japan where (assuming no selective migration) a phenotypic change not associated with a genotypic one was found; which is an example of the reaction range concept (Gottesman 1963, 1968) with the improved pre-and post natal environment in the USA Japanese promoting a changed phenotype. Two important axioms of the reaction range concept are the following: (1) Different genotypes may have the same phenotype and (2) different phenotypes may have the same genotype.

I feel the meetings will have been successfully only if: geneticist, psychologist, politicians and the like work together. to get an understanding of the problems of society and by working together resolve the ills which are working to destroy this society.

"Genetics"
Shirley C. Jackson
November 1, 1971

BENEFITS AND LIMITATIONS

The C. O. B. R. E. Reserach Workshop on Genetic Endowment and Environment in the Determination of Behavior took place at Wainwright House, Rye, New York during the week October 3-8, 1971. Students of "Genetics" of the Natural Sciences Department of the New York State University at Purchase were invited by Dr. Lee Erhman to attend as many of the meetings as we could manage. Because of other commitments, I only attended parts of the sessions on October 6 and 7.

Due to other class schedules, most students were able to attend only a limited number of these sessions. This discrepancy, undoubtedly, gave us a fragmented view of the total picture. The lack of proper preparation in the psychobiological sciences was another factor which limited our benefiting from this unusual opportunity in an academic sense. This gap might have been bridged partly if it had been possible for us to have a prior reading of the papers presented by the various scientists for discussion.

Despite the limitations mentioned above, I believe most students were able to followed intelligently a number of the arguments presented. The defining and redefining of familiar words (i.e. race, culture, etc.) from a scientific perspective, was most enlightening. In general, I think the students gained a broader and more realistic view of the various problems involved in basic research in the fields of behavior and genetics. The experience of meeting and conversing with such a large number of eminent scientists was awe inspiring.

As far as the scientists are concerned, it is perhaps superfluous for me to reiterate that, undoubtedly, the interaction and coordination with fellow scientists of related and unrelated fields benefited every participant. The opportunity to exchange ideas, update information and solve problems in group should be provided regularly tothose involved in serious research.

PERSONAL IMPRESSIONS

I came away with the impression that the everpresent contrasting views of geneticists and environmentalists are as alive as ever; and that basic research in genetic-environment interaction and behavioral adaptations should be accelerated to keep pace with and to provide data for the rapidly developing fields of genetics and behavioral science. There seems to be also a great need for basic data on the physiological explanation of behavior.

Risking oversimplification, and for whatever it's worth, my personal evaluation of the relative merits of genetics versus environment, is that:

Genetics gives us the basic disposition with which to react to the elements of the milieu in which we find ourselves. The individual that emerges from this is the summation of the interaction of his inherited characteristics and the multifarious experiences he encountered throughout his lifetime.

The environmentalists therefore should not assume the idea of an absolute tabula rasa at birth. There's no such thing as an absolutely clean slate from which environment could produce the desired creature. The best we could hope from environment is a controlled development or modification of the inherited characteristics of the individual toward the direction of recognized values of that given society.

OCTOBER 6

During the first day of my attendance, Mr. W. Pollitzer, described by fellow scientists as the anthropologist-geneticist-anatomist, led the discussion on the paper "Human Behavioral Adaptions - Speculations on Their Genesis", authored by Dr. I. I. Gottesman and L. L. Heston of the University of Minnesota.

According to Dr. Gottesman, the fact that behavior leaves no fossils created a real problem for the behavioral evolutionists who are forced to depend solely on analogous reasoning and debatable evidence. Methods for determining the sequential order of amino acids in proteins have been devised to help these scientists in their study of evolution. This is based on the fact that many mutations result in the substitution of one amino acid for another in the completed protein. The detection of such changes makes it possible to trace variations in a protein through a group of organisms. In this manner, it is hope that a behavioral evolutionary timetable could be established.

Perhaps this evolutionary protein clock could also be used to deal with evolution of brain size as a reflection of ecological or behavior demands.

Evolutionary significance of the variability in lactase production was discussed as an outstanding example of interaction between environment and genes. The distribution of phenotypes provides a model of divergent evolution based on a cultural-technological advance and a change in gene frequency.

OCTOBER 7

On October 7, the paper "Gene-Environment Interactions and the Variability of Behavior", authored by Df. L. Erlenmeyer-Kinling, was discussed by Dr. W. Thompson in the morning; and "The Meaning of Cryptohomunculus" authored by Dr. E. Tobach was discussed by Dr. A Jenkins in the afternoon.

The mechanics and difficulties of investigation of gene-environment interactions posed various problems. The consultant, Dr. Erlenmeyer-Kimling raised the question of the devising of parameters for our investigation. The inability to accurately define or single out the whats, whens, hows, and who's we are measuring, gives most investigations an indeterminate quality. To illustrate her point, she asked: "What shall we say is man's 'natural' environment?" and "From what baseline can we speak of deprivation, enrichment or inadequacy of stimulation during infancy and early childhood?"

"Behavior, like all other biological phenomena, is a function of genetic processes," admitted Dr. Tobach, psychologist of the American Museum of Natural History. She added, "There will probably be the most disagreement about the role of these genetic processes in the highest level of behaviors integration known to us at present: the behavior of human beings in a technologically complex society."

She attempted to explain the complex steps of integration on different levels of organization of gene function and a behavior pattern, in the following manner:

"At every level, the 'interaction' (gene-environment) is changing and fusing into a 'new' genetic-functional substrate which is in a new relationship to a new 'environment.' The events at one level of organization at one point in time is the substrate from which the next developmental sequence is generated. As the changes between levels become incorporated, the original configuration changes its relationship to the level under focus. The change is not additive -- it is a change in quality as well as in quantitative aspects."

In closing, I'd like to borrow an allegorical passage from Dr. Gottesman: "Homo sapiens in all our glory has evolved as a conglomerate of compromises; it is not a form of condescension to deal with members of our species via compromises. It is rather a cultural adaptation required by our genetic adaptedness."

RESEARCH WORKSHOP

ON

GENETIC ENDOWMENT AND ENVIRONMENT IN THE DETERMINATION OF BEHAVIOR

by

Judith Beth Stone

S.U.N.Y. at Purchase

Dr. Lee Ehrman

November 1, 1971

I attended two of the meetings of the Research Workshop. Though unprepared academically (having had only three class periods in Genetics prior to the meetings), I did benefit from this fortunate opportunity. I was able to meet with informally and listen to in discussion some of the most highly qualified and dedicated geneticists in the world. I was pleased to find a group of scientists who derive satisfaction from their challenging and important work; who, though their experience and opinions are diverse, were able to converse about a significant, controversial and problematic topic; and above all, who were wonderful human beings, some of whom made a deep impression on me.

The question of "acquired vs. innate" characteristics is very old and still unsettled when applied to behavior. The difficulties in approaching the problem in human beings are almost overwhelming. Still it holds the attention of scientists because of the value of its answers to so many fields, including education, food and nutrition, social work, psychology, environmental science and of course genetics. I don't know if at the meetings any definite agreement was arrived at, for any question that was approached brought on a subsequent debate usually ending where it began. But not without purpose. The scientists learned from each other, and the students learned from all.

On the first day of the workshop, I attended a discussion of Claudine Petit's paper,"Qualitative Aspects of Genetics and Environment in the Determination of Behavior". The other paper read and heard discussed is "Biochemical Genetics and the Evolution of Human Behavior" by Gilbert S. Omenn and Arno G. Motulsky. I found the latter paper largely incomprehensible, having very little knowledge of biochemistry. Its value for me lay in the vast area it covered and any bits of information that I could extract to contribute to my knowledge of biology, chemistry, and anthropology. Claudine Petit's paper and the discussion pertaining to it were far more valuable to me in sorting out my thoughts and coming to some conclusions about the subject of this workshop. This is because her paper was more intelligible to an undergraduate student and because she seemed to come to grips with the problem in a direct way and give some answers backed very solidly by evidence.

She begins by presenting her topic: Are behavioral traits coded in the genes or acquired through interactions with the environment? She so quickly and with apparent simplicity "solves" the problem when she says, "I, as a Geneticist, think that it is a false problem; everything, at bottom, is a matter of Genetics", that her reader may doubt her credibility at first. My respect for Ms. Petit was soon restored as I read on to learn. of the significance of non-genetic factors (the physical, biological, and social environments) in the determination of behavior. The environment may intervene at a critical period, during embryonic development or growth, when the genetic channel corresponding to a particular behavioral trait is open.

Though the impact of the environment is dependent upon what is already coded in the genes, its significance must not be undervalued considering the number of genetic channels and environmental influences that can operate (especially in man where culture serves to compound the influences of environment). Genetics and environment are interrelated and interdependent. The final manifestation of character in the phenotype is a result of genotype and environment (its own freedom to affect a change being dependent on the genetic code).

The paper is divided into three parts. The first is "Genetic Determinism and the Influence of Physical Environment on Some Behaviors". In this section Petit deals with monogenically and polygenically determined behaviors and the way environment may affect those behaviors. Her brief discussion of Mendelian gene dependent behaviors, enforced by examples, illustrates behavioral genetics in its simplest ~~form,~~ the traits are determined by genes on a single loci, and are independent of environment. Behaviors of polygenic determinism, such as geotaxis and phototaxis, are more complex. The exact chromosomes involved with taxis have been discovered. But taxis are not independent of environment. For example, a certain beetle who is positively phototactic in the spring at temperatures from 10°-35°C is negetively phototactic above and below this temperature.

Sexual behaviors are important objects of study, since they directly affect speciation and maintian genetic variability among populations. They are polygenically determined. The courting behavior and physiology of Drosophila melanogaster was observed and experimented with. It was found that the receptors of the female are essentially on the antennae, while those of the male are scattered all over the body. ~~This fact~~ explained the sexually dimorphic behavior during courtship. In this example behavior is determined indirectly by genetics, through physiology and according to sex.

Vibration is a very important component of courtship in Drosophila. All of the elements of the physical environment that act on vibration have their effect on sexual behavior. Correlations were demonstrated between the mean frequency of vibration and body temperature, and between vibration frequency and the ratio of the volume of flight muscles and wing size. The temperature of the surrounding environment has its influence on sexual selection and isolation. Light, too, has its effect. For example, inablity to mate in the dark or sensitivity to light may put an individual at a sexual disadvantage.

The middle section of the paper deals with the way the action of genes may be modified by different physiological factors and hormones. Physiological factors dependent on rearing conditions, age and composition of blood are able to change sexual behavior in Drosophila. Flies reared in overcrowded conditions are at a disadvantage when competing sexually with overfed flies. Sexual maturity appears at different ages in various species of Drosophila, and sexual activity can change during the lifetime. these factors are influenced by hormones. In mammals steroids are able to change genetically determined behavior patterns. Through experiments with guinea pigs (castrating them, then injecting them with testosterone propionate), it has been proved that differences in sexual behavior are not the result of different amounts of hormones but are due to different responses of the tissues involved to the sexual hormones. These responses are genetically decided.

The final section of the paper deals with imprinting, learning and the advantage of the rare type. This section, in particular, because of its concern with the social and cultural environment, leaves the most questions unanswered. Here the problem of "nature vs. nurture" presents itself most obstinately. Ms. Petit directs her attention to animal experimentation hoping that some finds may be applied to human beings. She begins with imprinting, a phenomenon concerned with the first social ties in young animals which have an important influence on the social behavior of the adult. For example, a duckling will follow the first moving thing he sees after birth, and he will treat it as if it were his mother even if it isn't. The consequence of this early tie is a disturbed adult social behavior; the duck may court this object. Imprinting occurs at a precise stage of development, this critical period being genetically determined. The final resulting behavior is dependent upon the enviornment. (In this case the environment is the object that happens to be there at a ducklings birth).

Learning in cats was studied. It was found that genetically determined sexual behavior, released by hormones and developed by experience, continues even if the hormones have disappeared. If applied to humans, this would help explain sexually dimorphic behaviors as learned through our culture.

The sexual advantage of the rare type has been demonstrated by Ehrman and Petit in laboratory experiments using Drosophila. The reasons why the rare type is at a sexual advantage are not known, but it is an interesting phenomenon and can be observed in human societies. Lee Ehrman brought up the point that we all select rare and special mates. No one is attracted to the common type. This rang true and was well appreciated. Someone else mentioned the popularity of blondes in Arab nations, and the prefer~~er~~ence of dark, curly-haired individuals in the Scandinavian countries. Such examples of the advantage of the rare type, though unscientific as they may be, have the advantage of being observable in nature.

In conclusion, behavior is a matter of genetics. The environment may influence the way in which the genes express themselves; the genes also produce an inheritable potential to learn what isn't present in the genes verbatum.

The assignment of the paper was presented in the vaguest terms. I wasn't quite sure how to approach it. Not knowing wat was to be gained by the reader of this paper written by such a novice "geneticist", I decided to approach it in a selfish way; to learn what I could about the determination of behavior. It has been successful in my terms. I hope that in some way, whatever it may be, it will be profitable to the readers in Washington.

Report on COBRE Research Workshop on Genetic Endowment and Environment in the Determination of Behavior

Alcinda Lewis
Genetics
Dr. Ehrman
November 1, 1971

I attended all of days I and III, the afternoon of day IV, and the morning of day V of the COBRE Research Workshop on Genetic Endowment and Environment in the Determination of Behavior held October 3 - 8. I had at that time no real preparation for the meeting beyond a few weeks of a first genetics course and some reading in behavioral genetics. The papers which were presented were not available before the meeting to students. As a result, much of the work presented and the ensuing debate was obscure to me, but I did form some impressions of what issues are presently thought important, of the various positions which can be taken on these issues, of the folly of taking concerted action with little knowledge of a problem, and more generally, of the whole problem of determining whether a certain behavioral trait or pattern is generated by genes or by environment. In retrospect, I consider the experience to have been invaluable to me.

I naturally related to that part of the discussion which was concerned with human behavior (if I were to attend a similar meeting now, I would be much more attentive to the flies and rats) and much of the discussion seemed to be concerned with relating the behavior of these animals to that of man. I found parts of Gilbert Omenn and Arno Motulsky's paper "Biochemical Genetics and the Evolution of Human Behavior" enlightening as they mentioned five possible sources for research in human behavior: sexual dimorphic behavior, inborn errors of metabolism, inter-racial differences, polymorphisms of EEG phenotypes, and the effects of psychopharmalogic agents.[1]

(1) There is at present much concern with the differences in behavior between males and females and especially with the roots of the differences: cultural, genetic → hormonal, or both. Research was cited in the paper which indicates a relationship between certain hypothalmic regions, definitely effected by sex hormones, which "might be involved in neural motivational systems."[2]

(2) Of the enzyme deficiencies in man, those which are intrinsic to the nervous system are of course the ones which effect his behavior and have far-reaching consequences. The Lesch-Nyham syndrome, due to a deficiency of an enzyme which has its highest activity in the basal ganglia of the brain,[3] results for some unknown reason in a self-destructive, impulsive behavior. Homocystinuria, another such disease, might result in a higher probability of schizophrenia in the afflicted and his siblings. Omen and Motulsky suggest[4] that the documentation of any mild abnormalities in carriers for the many rare recessive diseases "might be useful in interpreting the range of normal behavior."

(3) Racial differences in behavior was a topic of frequent discussion at the conference. Work by Freedman and Freedman on new-born infants of Chinese-American and European-Americans is mentioned in the paper which was in support of old stereotypes of adult behavior: the Chinese exhibited calmer, less changeable behavior. The value of this work seems to lie in its being done on such young subjects as cultural forces

would tend to obscure work done on older ones. Differences in various proteins (in the blood) and enzymes in the brain between oriental, negroid, and caucasoid populations are known[5] and indicate that research in other differences might have some validity.

(4) Another area where work could be done is in the behavior of people with similar electroencephalographic (EEG) patterns. Individuals of either of two variant groups tend to marry one another. Individuals of another variant group might show a predisposition to psychiatric disorders. It would also be beneficial, as suggested in the paper, to correlate EEG patterns with reactions to various drugs.

(5) The evidence for the variety of response shown to different drugs by different people is brought up, along with the warning that since this variety does exist, and since analysis of hyperactive behavior is difficult, the widespread use of amphetamines and methylphenidate on schoolchildren should not be undertaken without much "attention and control."[6] The infinite variety shown by human beings, biochemically and therefore possibly behaviorally, is a theme which runs throughout the work.

In addition to the evidence for the genetic basis of behavior is the evidence for prenatal influences. The problem of so-called "noise" in the prenatal environment was brought up on the fifth day of the conference, and the value of definitely determining that a trait is not genetic - and correlating the differences in developement with behavior differences in dissimilar populations was stressed.

The argument for the powerful impact of environment was continually asserted by some participants in the conference and the question of whether one can ignore this force in making determinations of intelligence differences between the races was continually brought up. Then the question is which environment, home or school, is most important in determining IQ differences; the consensus seems to be with the home. One of the purposes, or possibly one of the results of the research in differences between people would be to tailor-make educational programs for certain types of people, or ones from the same economic background. This might lead to a segregation which would in the end defeat the purpose of the specialized training.

The sum of the arguments demonstrated to me that as far as human beings go, behavioral genetics has much to do; that there are tremendous problems in even testing for what you want to know; that there are many ways of looking at any situation; that populations must be looked at as entities.

Footnotes

1. Omenn, Gilbert S. and Motulsky, Arno G. "Biochemical Genetics and the Evolution of Human Behavior", p. 27-35.

2. Ibid.,p.29.

3. Ibid., p. 31.

4. Ibid., p. 33.

5. Ibid., p. 34.

6. Ibid., p. 37.

THE C. O. B. R. E. RESEARCH WORKSHOP.

October 3-8, 1971

Laurel Hall
S.U.N.Y. College at
Purchase.
New York.

I am a junior year student at the S.U.N.Y. college at Purchase. As a beginning student in Genetics, I had the priviledge of attending the C.O.B.R.E. research workshop on Genetic Endowment and Environment in the Determination of Behaviour.

First, I am not qualified to offer criticism of the genetic approach due to my generalized background in biology. Neverthelesss there are some observations which I deem necessary to comment on.

Scientists, especially those in behavioural genetics, after the publication of their finding in the laboratory have an impact on the society which at times becomes a threat to the average layman. Nature and nurture play an important role in behaviour and learning. The psychologists are presently seeking tools with which to nuravel the phenotypes involved in behaviour. This is a favourable situation. Behavioural Geneticists can speculate on the genotypes but until such ? time psychologists have not developed the qualitative means consequently the effect of the genes in behaviour of human cannot be accurately determined. It is analogous to reasoning how B is derived from A when there is no clear vision of A. Human behaviour is still in a state of infancy, therefore when experimenting and then publishing, caution becomes a necessity.

Clearly the work of the geneticist depends on the psychologist. A common bond is necessary for their communication as research scientists. Several times it became quite obvious that the concept or terminology , for instance, Natural Selection and Schizophrenia, as applied by a scientist was not clear in concept to the others.

Of special interest was L. L. Heston's research on Human Behavioural Adaptations -Speculations on their Genes. In the section on milk tolerance, his approach was rather simplistic in saying that milk intolerance was probably old- 10-12 thousand years and moreso when he used animal husbandry to account for increase in tolerance. The variables he used in the breakdown of lactose tolerance was in two broad categories- white Europeans and non-whites. Three allelles which seem to govern milk tolerance which in 1) infant can be fatal, 2) childhood can affect inteligence and 3) adult no effect on gene pool. It appears to be a better comparison in taking the three groups viz, infant, childhood and adulthood and showing the effect on gene pool. Mention was made concerning whole milk. But what of tolerance for milk products?. A breakdown of milk products for hreding and non-herding geographic areas would also be befitting.

In the presentation of E. Tobach's research on the Meaning of Cryptohomunculus , his discussant A. Jensen commented on

III

I.Q.level. Experiments with Blacks and Whites of the Northern and Southern American States do not provide valid measure of relative I. Q'S. If a valid measure of I.Q. ever becomes available, it must be applied to a more suitable situations than the above. Rather a private school where all races with similar socio-economic status, and controlling the variables as much as possible will give more accurate results. At this point it would be preferable for rigorous controls to be placed on environmental factors than to sacrifice these controls for the purpose of maintaining a larger sample.

The impact of behavioural genetics on societies cannot be a trial and error procedure. The importance of this branch of scientific study to the future of mankind cannot be overestimated. Should initial studies in this field direct societies to initiate programs to 'correct' that which ~~newr~~ ultimately never existed, it is possible that behavioural genetics which hold so much promise to improve man's lot may quite lead man in the opposite direction.

This paper is prepared for Mrs. Lee Ehrman
On November 1, 1971
For the course of Genetics
By Jacquelyn Villecco.
State University of New York, college at Purchase.

I am a student at the State University of New York presently studying under the field of Environmental Science. I have a very general background in science and very much interested in pursuing science as my major.

The Research Workshop on Genetic Endowment and Enviroment in the Determination of Behavior, which was held in Rye, New York during the week of October 3_8,1971, was the first opportunity I have had to communicate with intellectuals in the field of science. I was very impressed with the discussions, even though at times things were not very clear to me. The discussions were motivating to me as a student.

Another reason the research workshop was impressing to me is purely a personal reason. After one of the discussions, I was talking to a couple gentlemen, one of whom is W. Pollitzer, and the topic of discussion was my past schooling. I had mentioned briefly about the past college that I had attended and they both knew about the school. Why this is so surprising to me, is that I came from a little school in Michigan which is located out in the middle of nowhere. In my opinion, this showed a great concern on their part and it made me feel good.

There were many topics of discussion during this one week period and I would like to mention a few that had my complete interest.

The subject of height, under the topic of Human Behavioral Adaptations, was discussed and a good topic to select because it is controlled by both, genetics and environment. "The reaction range concept worked on by Clausen, Keck, and Hiesey (1948) obtained two important axioms: (1) Different genotypes may have the same phenotype and (2) Different phenotypes may have the same genotype." They came up with these axioms by planting different plants together and ones of the same kind in a different environment.

Some very interesting statistics were given relating to the reaction range concept with various height traits of Japanese children. They were given as follows:

13 year old Japenese girls:	Average height
in contemporary environment	146.1 cm
in post-war Japan(1950)	139.9 cm
born in U.S.A. with Japanese parents	150.5 cm
reaction range 10.6 cm	
15 year old Japanese boys:	
in contemporary environment	158.2 cm
in post-war environment	151.1 cm
born in U.S.A. with Japanese parents	164.5 cm

As one can see, the height trait must be under both genetic and environmental control. (It appears that if Japanese parents want their children to play basketball, they should come to the U.S.)

The Evolution of Milk Drinking, is also discussed under the topic of Human Behavioral Adaptations by I.I. Gottesman and L.L. Heston. Since avid milk-drinking was never one of my favorite past times this topic particularly interested me.

Lactase is an enzyme in the villi of the small bowel.

Human populations differ according to the amount of lactase present. In the absence of lactase, lactose (the main sugar in milk) passes through the system providing no nutrition. Cramps and diarrhea results from too much of this ingested lactose.

According to the Evolutionary Theory, lactose is benefical because it differs in amount from person to person. From studies, Asian, Amerindian, and African populations are lactose intolerant. It was also proven that European populations can consume lactose with little amount of trouble. "The proportion of tolerants is 90-100% in northern Europe and zero-10% in most of the rest of the world." (See map at end.)

It appears that this selection for lactose must have come about many years ago because milk products have been used since the domesticating of milking-animals.

These were a couple of topics discussed at the workshop and there were many more of a similar nature. I feel that there was a great communication among these behavioral scientists. Often this is not the case as such scientists sometimes ignore each others' research. This in itself is a great accomplishment. Nowdays we need times to get together and share our knowledge. And it seemed that this conference was just one of those times.

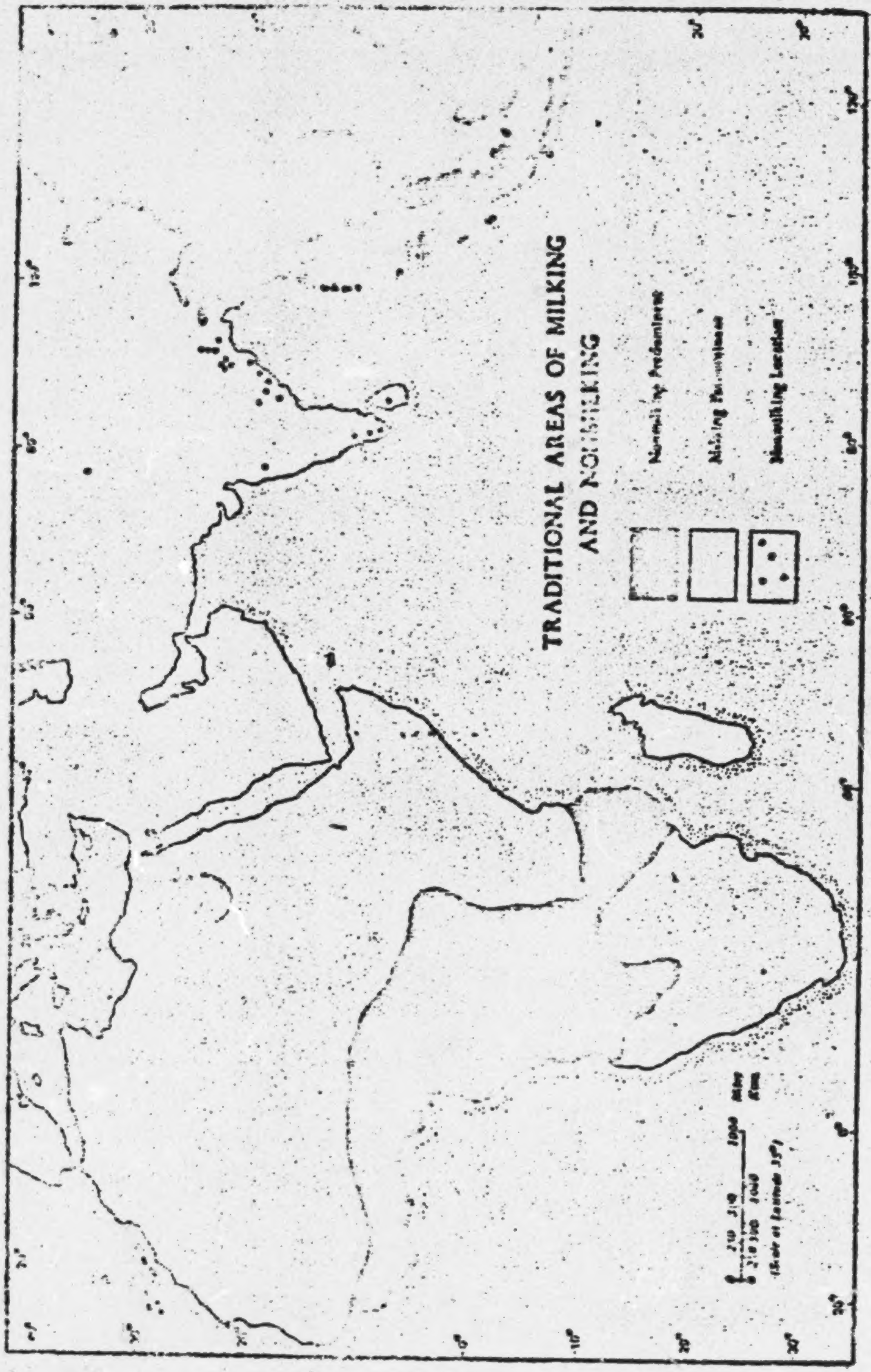
TRADITIONAL AREAS OF MILKING AND NONMILKING
Nonmilking Predominance
Milking Predominance
Nonmilking Location
250 500 1000 Miles
250 500 1000 Km
(Scale at Latitude 15°)

Fig 1. Traditional areas of milking and nonmilking.

from roughly 5500–2500
are uncertainties about
be the earliest evidence
where in the world. The
pastoral phase was rainier th
supported wild fauna such a
phant and rhinoceros, whic
today only in more humid
far to the south in Africa.
sufficient pasture for the ca
of the pastoralists. Ev
pastoralism derives both fro
excavation and from m
drawings that bear a strik
to the ancient cave pain
Spain. In many of the
animals and herdsmen are
there are no milking scenes.
ever, one scene, discovered
Mori, in the Libyan Saha
this scene to date from the m
ist phase (35), perhaps 4
clearly depicts a cow being
are other paintings for othe
Sahara, which also suggest m
none is as clear or convin
With the desiccation of the
about 2500 B.C. the past
Though the fate of the pas
certain, there are indication
some of them migrated south
There are, for example,
depicting pastoralists in
Somalia. Some scholars
present-day Fulani pastorali
African savanna, or certain
of East Africa (Kenya, Ug
ka) are descended from the
alists.

The southward penetrati
ism in West Africa was
widespread occurrence there
sleeping sickness, which
other domesticated animals
such penetration seems to

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An Attempt to Understand and Recognize Schizophrenia

by Paul Calantjis

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Abnormal behavior in man was discussed at the workshop. I was especially interested in the discussions that were concerned with schizophrenia. Some of the scientists of the workshop are working with people who are classified as schizophrenics. I am going to discuss the concepts and ideas of schizophrenia. I think it is important to point out that my attending the workshop and listening to the scientists discuss the subject of schizophrenia are two factors that have inspired me to write this brief reaction paper.

My intense interest in this subject is due to the fact that my mother has at times behaved in a schizophrenic manner. It is fairly easy for me to recognize this type of behavior, when it is present, over a long period of time. Since I am not a psychiatrist or a psychologist my attempts to describe schizophrenic disorders may not make scientific sense. However my definitions should make emotional sense and my definitions should reveal my feelings on the subject of schizophrenia.

Schizophrenia is defined in the Funk and Wagnalls Standard College Dictionary.

> Schiz-o-phrenia (skit so. frene-a) N. psychiatry- Any of a group of psychotic disorders characterized by delusional formations, a retreat from reality, conflicting emotions, and deterioration of the personality: formerly called dementia precox.

I should like to take this definition apart, word by word, and apply it to a real meaningful subject. I emphasize the idea of taking this definition apart word by word because the only way that I can make any sense out of this definition is by separating the definition into constituent parts or elements, so as to determine the nature of the whole by examination of its parts. I hope that the puzzle of a schizophrenic personality can be pieced together and be considered as a unit. By examining many of the parts or elements of a schizophrenic personality one can realize that no two schizophrenics are alike; and that each schizophrenic has his own story to tell.

The first part of the definition says, any of a group of psychotic disorders. To further clarify this definition I want to present some dictionary definitions of the words that make up this piece of the definition.

> group-collection or assemblage of persons or things considered as a unit.
>
> psychotic: fundamental lasting mental derangement characterized by defective or lost contact with reality

By examining the definitions of group and psychotic one could say that this part of the definition says that schizophrenia is any one of a collection or assemblage of fundamental lasting mental derangements characterized by defective or lost contact with reality.

The final and most important parts of the definition of schizophrenia tells one that these fundamental and lasting mental derangements are characterized by delusional formation, a retreat from reality, conflicting emotions and deterioration of the personality. I will attempt to further clarify these conditions by giving definitions and examples of these conditions.

Let us start with the concept of delusional formations. A closer look at the two words that describe this concept will help us to understand it better.

> delusion- a false belief regarding the self or persons or objects outside the self that persists despite the facts and is common in some psychotic states.

formation- an act of giving form or shape to something or of taking form

After examining these two word definitions one might conclude that a delusional formation is an act of giving form or shape to false beliefs regarding the self or persons or objects outside the self that persists despite the facts and is common in some psychotic states.

Let me give an example of delusional formation. Definition by example is extremely helpful in understanding the behavior of a schizophrenic. My mother, when behaving in a schizophrenic manner, would sit in a blue chair in the living room and say "I am the Blessed Virgin Mary, queen of heaven". Mother would repeat this statement over and over again. ~~I believe that~~

My mother is a Roman Catholic and she is familiar with the concept of the Blessed Virgin Mary. The Roman Catholic Church believes that Jesus Christ was born of a virgin. This virgin is called the Blessed Virgin Mary. According to the Church the Virgin Mary was a pure and holy women who was qualified to be the mother of Jesus Christ.

It appears to me that my mother saw herself as the pure and holy Blessed Virgin Mary. If my reasoning is correct this example shows that my mother was giving form or shape to a false belief regarding herself despite the facts. The facts being that she is the mother of three children and not the mother of Jesus Christ.

The idea of a retreat from reality is another characterization of schizophrenic behavior.

> reality- that which exists; that which is real; actual things situations or events; that which exists as contrasted with what is fictitious or merely conceived.

> retreat- withdraw

A schizophrenic withdraws from actual things, situations or events and tends to spend time thinking about that which is fictitious or merely conceived of.

At certain times my mother seems to retreat from reality. When not feeling well mother will withdraw from actual things, situations or events. Mother will not eat, she will do very little housework, and she will not make any effort to maintain her physical appearance.

Cpnflicting emotions is another part of the schizophrenic personality.

> conflict- emotional tension resulting from inner needs or drives that are incapable of being held by one person at one time.

> emotions- a state of feeling; a psychic and physical reaction subjectively experienced as strong feeling and physiologically involving changes that prepare the body for vigorous action.

Emotional conflict is a condition where a person experiences strong feelings and physiological changes because he is unable to satisfy his urgent basic needs or drives.

If one looks closer at the definition of conflict, he will find that the word drives is used.

> drive- an urgent, basic, or instinctual need, an impelling culturally acquired concern, interest, or longing.

Going one step further we find that the word culture is used in the definition of a drive.

culture- the act of developing the intellectual and moral faculties, especially by education.

Since a drive is an impelling culturally acquired concern and culture is the act of developing the intellectual and moral faculties, especially by education it is reasonable to assume that some drives are satisfied by education. Education involves teaching and instruction by another person. My point is that an impelling culturally acquired concern or drive has to be taught to you by someone else if it is to be a culturally acquired concern. If a drive is not taught to a person then that person may not be able to experience that drive. People teach and instruct other people to experience some drives.

Now conflict occurs when drives are not satisfied. A conflict may occur if someone fails to teach or instruct another person to experience a drive. The schizophrenic person who has emotional conflict has not been able to fulfill his culturally acquired interests. Very few people have taught or instructed the schizophrenic to experience drives. In other words very few people have taught the Schizophrenic to help himself.

– Schizophrenics are human beings who have urgent, basic needs. Schizophrenics need people to talk to and to communicate with. Schizophrenics, as well as all human beings, have a need to feel free from fear or anxiety. To satisfy his basic needs a schizophrenic must be able to communicate and interact with his fellow man. A schizophrenic, just like any man, can get by with a little help from his friends. I feel that the best way to make life more bearable for an individual is to help him to help himself.

Let me attempt to clarify my opinions by bringing my mother into the picture. I believe that if I can teach or help my mother to become aware of her own states and processes, she will be able to help herself.

My mother gets depressed when she has nothing to do, or when she does not want to do anything. She will sit in the blue chair in the living room all day long. She clicks her teeth and she leans over and rests her head on her hands. My father is at work and my brother and I are in school. Mother has no one to interact with; her culturally acquired concerns or drives are not being fulfilled.

When my mother has someone to interact with her life changes. I became interested in painting the inside of the house. I bought some baby blue latex paint and painted my father's bedroom. My mother saw me painting and asked if I wanted help. I went down to the cellar and got her a paint brush. Mother painted the banister the stair case and the bathroom trim. Mother said she liked to paint. With my mother and I painting we accomplished much more than I had expected to do by myself. My mother and I accomplished something as a result of our interacting. This interaction was beneficial to both of us. We were able to fufill some of our basic culturally acquired interests or drives. If people can help one another to become more aware of their own states and processes they will be able to help themselves.

My mother likes to work with flowers. I wanted to learn the names and types of flowers. Mother asked me to take her to the Sterling Farms Garden Center. Throughout the spring and summer I would drive with my mother to the garden center and buy petunias, gardenias, mums, roses, vincas and many other flowers. We both enjoyed planting flowers and making a flower garden by the front of the house.

At present my mother is feeling well. She walks into the village, she does not have a driver's license, and goes shopping in a store called Whats New. She paints various parts of the house. She walks downtown to the beauty parlor to get her hair washed and set. She stops in the Sloatsburg inn and she buys coffee. She is interacting with people and she seems to be fufilling some of her drives.

The idea of interacting in order to fulfill culturally acquired interests is a very important concept that scientists, and psychologists should consider when working with schizophrenics. Scientists, psychologists, and schizophrenics are human beings who can fulfill one anothers drives if they interact with one another.

The final part of the definition of a schizophrenic personality tells us that the schizophrenic's personality deteriorates.

> deterioration- falling from a higher to a lower level in quality, turn downward with a consequent loss of vitality or energy
>
> personality- the totality of an individual's behavioral and emotional tendancies: organization of the individual's distinguishing character traits, attitudes, or habits

The organization of the individual's distinguishing character traits, attitudes, or habits fall from a higher to a lower level in quality with a consequent loss of vitality or energy.

It is easy for me to recognize the above type of behavior when I see it in my mother. When feeling well mother communicates with the people in her environment. She tells me that her gardenias are blooming or that she just bought a new type of cleaner that foams. When feeling well mother wants to do something. She tells me to buy her paint so that she can paint the kitchen cabinets, she asks my father to take her out for coffee. Mother smiles and laughs when she is feeling well.

On the other hand when mother is depressed her behavioral and emotional tendancies as a whole deteriorate. She sits in her blue chair and she smokes cigarettes. She seldom mentions her flower garden. She talks to herself. She does not feel like doing anything and she has a loss of vitality or energy.

I hope that the ideas, concepts and examples in this paper give some understanding of the inner nature of schizophrenia. I think that it is important to mention once again that schizophrenics are human beings who need a little help from their friends. Schizophrenics can help man to satisfy his culturally acquired interests or drives. I want to express a personal need for more genetic and biochemical knowledge about schizophrenia so that I may test some of the generalizations that I have made about Schizophrenia. Finally I want to say that my mother is an intelligent individual who has helped me to satisfy many of my culturally acquired interests or drives.

I want to thank Doctor Lee Ehrman, my genetics teacher, who made it possible for her class to attend the Wainwright meetings on Genetic Endowment and Environment in the Determination of Behavior. Communicating with the scientists who attended the Wainwright meetings was a rich and rewarding experience that I shall never forget.

RESEARCH WORKSHOP
ON
GENETIC ENDOWMENT AND ENVIRONMENT IN THE DETERMINATION OF BEHAVIOR

October 3-8, 1971

for

Dr. Lee Ehrman
State University of New York
Purchase, New York

by

Carol A. Krueger

Nov. 1, 1971

Introduction

I am a junior year student at the State University of New York at Purchase. I am presently enrolled in my first course in Genetics under Dr. Lee Ehrman, and was privileged to be invited to attend the Research Workshop on Genetic Endowment and Environment in the Determination of Behavior at Wainwright House in Rye, New York. My prior education in Natural Science contributed to my understanding of the proceedings, however, my knowledge in the field is limited.

Sessions Attended

I attended two sessions; "Qualitative Aspects of Genetics and Environment in the Determination of Behavior," Claudine Petit, Consultant and Aubrey Manning, Discussant, and "Human Behavioral Adaptations - Speculations on Their Genesis," I.I. Gottesman and Leonard Heston, Consultants, and William S. Pollitzer, Discussant. I also visited at luncheon with G. Omenn, Steven Vandenberg and Claudine Petit.

Overview - Impressions

On a whole, after attending the Workshop, I gained an appreciation for the field of Genetics and a great respect for the capability and intelligence of the people involved in researching this field. The scope of the field both in breadth and depth is greater than I had initially anticipated, given my limited knowledge. I sensed, both in the formal presentations and the informal conversations, a great sense of not only dedication but of enjoyment on the part of those pursuing further knowledge and its subsequent application in this field. This was very interesting and helpful as well as stimulating to me. Stimulating in the sense that I would like to share in the obvious satisfaction that these people find in their respective and collective interests. As the sessions progressed, I was able to more fully appreciate the great strides that have been made in the evolution of Behavior Genetics. I have been encouraged in my perception of behavior to include both genetic evolution and environmental adaptation.

Benefits of Attending the Workshop

For a beginning student in Genetics, attending the sessions was of benefit both in learning and experience.. Listening to the discussion of the presented papers was of great interest, and the subsequent interpersonal interaction of the delegates in formal sessions and informal luncheon situations were a valuable experience. The interest in the students attending shown by the delegates was very gratifying. Continuing reflection on the proceedings is stimulating. Personally, the net result of this unusual opportunity has been to heighten my interest in Genetics and to renew my enthusiasm to continue study in this field.

Limitations in Attending the Workshop

First, it was evident that my academic background had not prepared me to gain the most from attending the discussions. An opportunity for exposure to the material beforehand would have been advantageous. Secondly, the number of sessions I attended and the period of time in the sessions per topic were personal limitations. Although, I realize that the Research Workshop was not held solely for students, a previous course in Genetics would have been helpful.

In summary, the opportunity was invaluable from any perspective. I appreciate the invitation to attend.

Research Workshop

on

Genetic Endowment and Environment in The Determination of Behavior

Report done for
Dr. L. Ehrman
by
Brenda Brewton

Brenda Brewton, formerly a student at the Mt. Vernon, Cooperative College Center, A Division of S. U. N. Y. College at Purchase. I am now a junior at the College at Purchase, Purchase, New York. My field of concentration is Biology, and I am presently studying Genetics under Dr. Lee Ehrman.

During the week of October 3 through 8 I attended the Research workshop on Genetic Endowment and Enviroment in the Determination of Behavior. The workshop was held at Wainwright House, Rye, New York. Ernst W. Caspari, Workshop Director and Lee Ehrman, Workshop coordinator.

Unfortunately, after having been a student in Genetics for only a week, we attended the workshops on Genetic Endowment and Environment in the Determination of Behavior. Because of my limited Genetic background, I found it difficult to follow the discussions due to the terminology used. Due to other academic demands I was unable to attend all session, however, the ones I did attend I found to be quite a fruitful experience.

This paper will simply deal with those topics that I found interesting during the general discussions of those sessions which I attended. My conclusion will be my reaction to the sessions as a whole, as a begining student in the field of Genetics.

Day I (P.M.) Qualitative Aspects of Genetics and Environment in Determination of Behavior. Consultant - C. Petit Discussant- A. Manning.

The main point brought out by Manning was the experiment~~s~~ on the songs of birds. If a bird is deaf before he begins to sing ~~it~~ he will sing for the same length of time and probably in the proper key, but it will be rough sounding. This however, would seem to be a contradiction of the finding of Dr. Petit. In her paper Petit states "In the first series of experiments birds normally raised by their parents were separated from them in September, in order that they might study their songs the next spring. If the young were exposed to all birds songs during development, such as Chaffinch and other species, their song was normal. If the young w~~as~~ere exposed to no other birds except their companions from September to May...the result was different: Ph~~r~~ase I and II were normal, but Ph~~r~~ase III, specific to each community of young birds, was slightly abnormal. In a last series of experiments, the birds were hand reared and never allowed to hear an adult song; Phrase I and II were correct, but Phrase III was partly or completely lacking. Each community has an entirely individual, but extremely uniform, community pattern."

The summation was that the gene~~s~~ expressed in Ph~~r~~ases I and II is considered to be fixed expression. The modulated elements of ph~~r~~ase III are learned during the social ph~~r~~ase that follows birth. They can be considered as a phenotype manifestation, developed, perhaps, by sexual selection.

Day II Arrived at Wainwright House in time for afternoon session but it had been postponed until that evening.

Day III (A.M.) Human Behavioral Adaptations - Speculations on Their Genesis. Consultant: I. Gottesman - Discussant W. Pollitzer.

The highlight of this discussion was "Another trait in which human populations differ is the concentration of the enzyme lactose. It is the only common trait known at both the biochemical and behavioral levels that contributes to "normal" variability in both."

"Lactase is an enzyme active in the villi of the small bowel and lactose is the main sugar in milk. Lactase splits the disaccaride lactose into the monosaccarides glucose and galactose. Monosaccarides can be absorbed into the portal circulation but disaccarides cannot. In the absence of lactase, ingested lactose simply passes through the gut without providing nutrition. If too much is ingested, cramps and diarrhea result."

During the discussion it was revealed that the public generally, assumed that the reason black people did not drink milk was because they were ignorant of its nutritional value, rather than the fact that their genetic make up promoted an intolerance of it.

It was also noted that the tolerance for lactose is common among Europeans and that Asian, Amerindian, and African population on the other hand are generally lactose intolerant.

Day III Biochemical Genetics and the Evolution of Human Behavior. (P.M.) Consultant G. Ommen and A. Motulsky Discussant V. Anderson.

The topic that dominated this discussion was"Current Studies of Enzyme Variation in Human Brain"

"Deficiencies of seven of the glycolytic enzymes have been identified as causes of hereditary hemolytic anemia in man... Deficiency of the other enzymes was not associated with any neurologic abnormalities. Such tissue~~s~~ comparisons are important for another reason if the same gene is responsible for the enzyme in all tissues, sampling of blood or skin or hair follicles may enable us to test for properties of the brain enzyme without needing to obtain brain tissue."

Dr. G. Ommen who is presently doing research on the Human brain; receives the brains from 2 to 48 hours after the death of a patient. He had 150 specimen~~t~~s of which 132 were Caucasian. It was also brought out in the discussion that the concentration of enzyme in the basal gangia of the midbrain seemed to be more evident amoung those patients that had commented suicide.

Day IV Gene - Environment Interaction in Determining Behavior Consultant:E. Tobach, Discussant: A. Jensen (P.M.)

I arrived late - after what seemed to have been a rather lengthly discussion on the term "race". The group arrived at the conclusion that the word race would not be used, but simply referred to as a population.

During this discussion Jensen was giving'some' poor justications for the uses of I.Q. tests. However, the most important topic of this discussion was "pushed under the table", That was Dr. Tobach's concern as to whether the scientist would be responsible for how society uses his research.

Day V - Did not attend.

Behavioral Genetics is a field of study that incorperates aspects of both psychology and biology. A societies structure may be defined as the ordering of the behavioral patterns of the individual members of that society. Therefore, it becomes obvious that the study of behavioral genetics will serve to wed science and society more closedly than they have been joined through mere technology.

Though scientists would like to maintain their sacrosanct objectivity, they are in the final analysis products of a society and subject to all of the pressures of that society. The problem of maintaining objectivity is more critical to the worker in behavioral genetics than to workers working in other fields of scientific endeavor.

A patent example on societie's encroachment on scientific discussion arose in a dispute at the C.O.B.R.E. meetings involving the term 'race' . The participants in the discussion finally decided to use the term population instead of race.

It is most unfortunate that the question raised by Dr. Tobach on the responsibility of the scientist to take an active interest in the uses to which society puts his research came so close to the cocktail hour as to sharply curtail any meaningful discussion. Their attitude of "I'm a scientist, not a humanitarian", is no longer a sufficient excuse for disregarding the uses to which society puts their work, particularly in the field of behavior. In as much as Darwin never conceived that his findings would be used to promote what is known as Social Darwinis~~m~~m, we can assume that the basis for possibilities in behavioral ~~G~~genetics may be misinterpreted and used for aberrant social and political purposes. Now, while the field is young and still seeking its direction, involved scientists should be made aware of their two fold responsibility. The responsibility is both ethical and moral; an ethical responsibility for accurate research, and a moral obligation to take an active interest in society's uses of that research.

If the scientists left the workshop with the realization of the ties it has with society - especially in the area of behavioral genetics and their responsibilities as scientist to society; then I as a begining student of genetics and a member of society can say that the workshops were profitable.

GENE-ENVIRONMENT INTERACTIONS AND THE VARIABILITY OF BEHAVIOR

by

L. Erlenmeyer-Kimling

Paper Prepared for C.O.B.R.E. Research Workshop on
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Introduction

The topic assigned for this paper is "gene-environment interaction in the determination of behavior." As Haldane (1946, p. 147) once noted, "the interaction of nature and nurture is one of the central problems of genetics." Most of us, I think, would surely agree that it is a central problem of the study of genetics and behavior. We would probably agree also on the 'ubiquity' of G-E interactions to be found in behavioral phenotypes (Lindzey et al., 1971). It is remarkable, therefore, that so little systematic attention, either in research or theory, has been paid to the implications, extent, and meaningful analysis of interactions. For instance, a recent review (Lindzey et al., 1971) that gives ample coverage of the literature relevant to behavior genetics in the past few years contains exactly one-half page (out of 40) devoted to the topic of interactions. This is not because the reviewers were remiss but because--with a few notable exceptions, such as research by several investigators on audiogenic seizures (cf. Fuller and Collins, 1970; Ginsburg, 1967), a series of studies by Norman Henderson (1968, 1970b), and theoretical discussions by Vale and Vale (1969) and by Harrington (1968, 1969)--workers in the field had given them little on which to report.

Perhaps we sometimes tend to be carried away by the complexities and the wide sweep of interaction possibilities. Perhaps it seems better for these reasons to refrain from fishing in such muddy waters. Yet, we do have quite a great deal of information about gene-environment interactions from other areas of biology and medicine; we do have some models to serve us.

We have had information for a long time about differential genotypic responses to a variety of environmental conditions in plants, bacteria, and even Drosophila. We know that the embryological effects of teratogens and other intrauterine insults differs within and between mouse strains, and probably within and between human genotypes as well (Fraser, 1963). We are familiar with a long list of heritable susceptibilities to infectious agents (Cox and MacLeod, 1962) and a growing list of genetic conditions that are associated with adverse reactions to certain drugs (cf. Vessel, 1971) or special foodstuffs such as the fava bean (cf. Stamatoyannopoulos et al., 1966). Rh-incompatibility of mother and fetus is clearly an interaction between the fetal genotype and the intrauterine environment provided by the mother's genotype. There is a lengthening list of metabolic errors that result in serious inabilities to cope with specific nutrients found in common foods, and some of these, like phenylketonuria and galactosemia, have behavioral concomittants.

In behavior genetics itself, work on audiogenic seizures in mice offers a prototype for studies of the interactions of heredity and environmental factors: some strains being highly seizure-prone and others not; some being capable of seizure induction and others less so; some being sensitive over longer periods and others over shorter periods; etc. All of the complications of dealing with interactions are there to be found in the audiogenic seizure research, but so are some of the uses to which analyses of G-E interactions may be put. For as Ginsburg (1958) and Vale and Vale (1969) and others have emphasized, the study of the ways in which hereditary and environmental forces work together can provide one of the most powerful tools available for learning about mechanisms underlying behavioral processes.

What Is Interaction?

What do we mean when we talk about genes and aspects of the environment interacting? To many behavioral scientists, interaction means chiefly that environmental stimuli must impinge upon a biological substrate for a behavioral response to be emitted. These students of behavior believe that, barring major genetic deviations such as those involved in inborn metabolic or neurological dysfunctions, experiential factors mold the phenotype pretty much independently of genotypic factors. To geneticists, by contrast, the keynote of interaction is that different genotypes may respond differently to the same environmental conditions. Relationships between genes and environment can be of several kinds, however, and not all are consistently called 'interactions.' My objective in this section will be to review briefly the several types of gene-involved relationships, to point to some of the overlapping between them, and to consider some of the difficulties that have arisen in attempts to classify 'interactions.'

The several types of gene involvements. Genes can take part in three basic types of interactions besides those involving what we usually think of as 'environment.' They are: interactions between alleles (dominance), between genes at different loci (epistasis), and between genes and cytoplasm (Mather and Morley-Jones, 1958). Of course, cytoplasm is itself a part of the nongenic environment, but usually these interactions are considered apart from the ones involving other environmental sources; not a great deal is known about gene-cytoplasm interactions. Although we are concerned here only with the relationships between genes and environmental factors, it must be remembered that interactions may be (in fact most likely are) going on at several levels at once. To take an obvious example, a phenylalanine loading test for heterozygote detection involves an interaction between an environmental manipulation (the administration of phenylanine) and the product of an allelic interaction--the allelic interaction itself usually being undetectable except following exposure to the environmental treatment.

When we try to break down complex behavioral responses into components, we are likely to encounter epistatic interactions, or at least the sequential action of different genes that affect different parts of a behavioral chain. One illustration can be found in Rothenbuhler's (1967) work with honeybees. Nestcleaning, that is, disposal of diseased larvae from the nest, consists of two successive acts (uncovering of the cell containing the larva and removal of the larva). Each step is largely under the control of a different gene, but the environmental stimulus, presence of diseased (or otherwise-killed) larvae, is the necessary trigger for the behavioral sequence to occur. One may imagine that courtship, mating and fighting patterns in many species probably entail even more complex feedback relations among several genes and successions of cues from a rapidly altering environmental situation. Perhaps attention to multi-level interactions of this type would not be highly rewarding; certainly, they would not if they led to an infinite subdivision into small responses and movements, each of which might be part of several other behavioral patterns (Scott and Fuller, 1963). In other contexts, however, examination of both intergenic and gene-environment interactions, and their interplay, might prove valuable. There are scattered indications, for instance, that heritabilities and dominance relationships are frequently altered over the course of learning processes. Do such changes, if they actually occur, merely reflect "progressive releases of the genetically determined response from the effect of environmental stimuli irrelevant to it" (Broadhurst and Jinks, 1966, p. 471), or, if heritability is decreasing, does the change reflect progressively increasing importance of task-relevant variables compared to genetic variables? Or do they perhaps indicate that different genes or different groups of genes take over at various stages along the way? To my knowledge, attention to questions concerned with such multi-level interactions has so far been scant.

Two relationships between genes and environment. Two types of relationships that occur between genes and environmental factors are frequently omitted from discussions of interactions. Both, though acting within the course of individual lifespans, have their main effects (usually) over the longer span of population-time. These relationships are natural selection and G-E covariance.

The fact that gene-environment interactions form the basis for natural selection is, I think, quite obvious. Natural selection, of course, refers to the fact that different genes (or, more precisely, different alleles of different genes) are transmitted to successive generations in different frequencies. Differentials in transmission frequencies may be attributable to inequalities in either survival or reproductive rates (or both) among the carriers of different genes. Whichever may be the case, the source of the transmission differentials is to be found in the patterns of interaction, more or less favorable, that the genes in question form with various aspects of the environment. By creating new interactions, changes in the environment can also change previously existing differentials in reproductivity or viability. As observed by Caspari (1967), selection for coadaptive gene complexes, rather than for individual genes, is probably the general rule--a point which bears upon the questions of multi-level interactions raised in the preceding section.

There is ample documentation (cf, Part I in Hirsch, 1967) for the role of behavior as one of the important interaction products through which selection, stability, and change may be mediated. One point may be worth reiterating here. Gene-environment interactions by creating selection differentials may change previously existing environmental conditions and thereby eventually reach new selection levels as well. For example, in Ehrman's (1970) research, Drosophila males with rare genotypes are found to have a mating advantage over males that are common in the population, so that through this selection differential changes can be introduced in the genetic composition of the population (which in this instance can be regarded as an environmental parameter) with the selection differential, viz., mating advantage, gradually diminishing as the population attains a balance between the initially rare and common genotypes. Analogies are to be found in the feedback chains linking human cultural developments, genetic factors, selection, and further pressures on the environment itself. For instance, the following hypothesis is suggested by Wiesenfeld (1967) in attempting to account for the relationship between sickle-cell trait, malaria and agriculture:

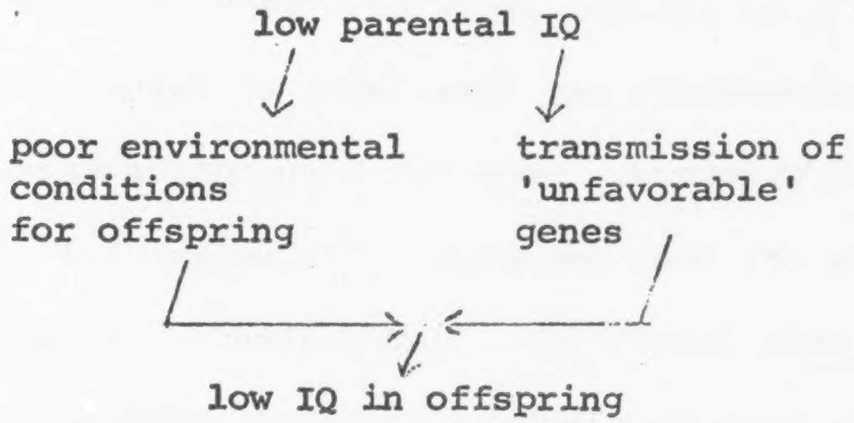
> "In the case of an intensely malarious environment created by a new agricultural situation, the variability of the normal individual is reduced and there is selection for the individual with the sickle-cell trait; this means that the nature of the gene pool of the population will change through time. This biological change helps to maintain the cultural change....(and) may allow further development of the cultural adaptation, which in turn increases the selective pressure to maintain the biological changes" (p.1139).

While natural selection is often not mentioned at all in discussions of interactions, covariance, the second relationship between genes and environment mentioned above, is sometimes formally excluded. Covariance means that genotypes are differentially distributed across environmental conditions, the most obvious example being the ecological distribution in nature of species, subspecies, and population groups to those niches to which they are best adapted. Sickle-cell trait and certain other hemoglobinopathies which presumably confer protection against malaria occur mainly in regions where malaria was formerly endemic; adult lactose intolerance appears to be confined to populations in which dairy husbandry never developed--or, perhaps, it should be said that lactose tolerance appears mainly in populations that did develop the practice of using milk products. These are two reasonably well-established illustrations of the covariance between environmental demands and human genetic variants. Covariance is the result of selection based on G-E interactions which have taken place at some time. Several cautionary comments must follow the foregoing statement. First, because we so very quickly move from natural to social selection, and social implications, when considering questions relating to covariance, I think it important to stress here that both interactions and selection always in reality involve the phenotype rather than the genotype. This, we all know, applies to every point throughout the present discussion, but it becomes especially crucial to emphasize the phenotypic basis in speaking of covariance. A second critical question is whether the basis for the earlier selection in any way correlates with the phenotypic character that is now under study. If population subgroups had been differentially sorted on the basis of physical strength or eye color or nose shape, we would expect to find covariances of subgroup and those characters that correlate highly with the selection criterion. But only those characters. Anything else that seems to be assorting differently into the groups defined by the original selection criterion must be either (a) chance correlations attributable to a 'founder's effect' (if the original population was small), (b) an effect of differential environmental treatments and G-E interactions in the various groups, or (c) experimental bias. A third important question is whether selection (mobility) has been maintained over time. As Haldane (1965, p. xcii) commented (probably with only partial accuracy): "If the sons of brahmans who could not learn the vedas and discuss philosophy had been expelled from their caste and made to sweep the streets, the brahmans might now dominate India completely." When rigid nonmobile class or caste systems have been operative, the covariance of most behavioral characters with caste is probably negligible, for, as Haldane continued: "In practice the efforts of members of every ruling group are largely devoted to preventing their children from falling in the social scale."

When social, rather than natural, selection is involved, it is exceedingly difficult to separate covariance and ongoing interaction effects. Two familiar teasers: (a) Are higher rates of schizophrenia found in lower socioeconomic classes because predisposed persons encounter greater environmental stresses in these classes (interaction) or because predisposed persons have downward social mobility (covariance) (cf. Dunham, 1970)? (b) Do IQ and social class have a positive correlation because environmental factors relevant to intellectual development are differentially distributed over classes or because phenotypic selection in the form of social mobility has produced different clusterings of genetic factors in the different classes (cf. Gottesman, 1968)?

Neither of the foregoing examples necessarily presents mutually exclusive alternatives between covariance and ongoing interactions. It is highly probable that both types of relationships between genetic and environmental factors are continually operating as Thoday and Gibson (1970) found in their "model experiment" on environment, mobility, and "class" differences in Drosophila.

It is possible that, within a generally similar milieu, individuals may be free to choose specific niches, certain features of the environment as opposed to others, or variations in behavioral patterns. Many of these differences in self-placements may correlate, at least indirectly, with genetic differences. Some may have consequences for later behaviors or, most important, for behavioral development in the next generation. For instance, Polansky et al. (1969) studying poor Appalachian families, have recently reported a positive correlation between mother's and child's IQs and also between mother's IQ and the adequacy of care given to the child. Investigators concerned with the effects of nutritional deficiencies or of perinatal complications upon intellectual development might consider whether similar within-group correlations are to be found between maternal IQs and nutritional adequacy of children's diets or between maternal IQ and precautions taken during pregnancy to protect the health of the unborn child. Thus, the inference commonly encountered in behavioral, educational, and medical literature is that poor prenatal, postnatal, or later rearing conditions are 'the causes' of low IQ (or various other unfavorable phenotypic outcomes). Without denying the significant, detrimental effects that such conditions impose upon development, we may also ask, however, whether the 'causal chain' contains a parallel and equally important link, viz.:


low parental IQ
poor environmental conditions for offspring
transmission of 'unfavorable' genes
low IQ in offspring

The point to be made here is that we run the danger, on one hand, of assigning too much weight to environment variables if we neglect the possibility that certain genotypes are more likely to be found in certain environments owing to selection based on phenotypic characters relevant to the ones that we may be studying. On the other hand, we must be equally alert to the opposite danger of overemphasizing hereditary influences by assuming that an observed covariance of genotype and environment necessarily bears upon the phenotype that we have under investigation.

Types of G-E interactions. In general we do not have in mind natural selection or G-E covariance when we talk about interactions. What we usually mean is that genotypes (or strains or populations) can be shown to react in different ways to the same environmental treatments. But how interactions are to be classified and what is to be done about them--on these points there is no solid consensus of opinion.

For many workers (cf. Haldane, 1946; Mather and Morley-Jones, 1958; Vale and Vale, 1969), the above description would be considered an adequate definition of interaction; any of the possible G-E relationships likely to be encountered in experimental data would be classified as 'interactions' by these investigators. Others (cf. Broadhurst, 1967; Lubin, 1961), however, would insist on the further criterion that delineates nonadditive relationships along the lines of the analysis of variance model. Thus, for interaction to exist, according to these workers, the amount and/or direction of the differences between genotypes must change over the various environments under investigation, "at least one set of means must be nonparallel to the others" (Lubin, 1961, p. 812).

Three basic types of G-E relationships can be distinguished as follows: (1) additive relationship where phenotypic differences between genotypes remain constant in all observed environments; (2) nonadditive relationship A, Lindquist's (1953) 'ordinal' interaction where quantitative differences in the phenotypic values change with different environmental conditions but rank orders do not change; and (3) *nonadditive relationship B, Lindquist's 'disordinal' interaction* where the distinguishing characteristic is a reversal of phenotypic rank orders as the genotypes are moved from one environment to another.

Now, the tradition of equating 'interaction' with nonadditivity grows directly out of the analysis of variance model which was originally designed to allow questions to be asked about 'main effects.' Interaction terms were later incorporated into the model to handle the realities of the natural world where the 'main effects' often do not add up in a simple fashion to account for all of the observed variance in the phenomenon under study. In spite of the provision for an interaction term, however, the analysis of variance model can create two sorts of difficulties for our understanding of the joint operations of genes and components of the environment.

First, significant interaction effects tend to be regarded by many experimenters as nuisance factors because the reason for using the model is still, in most cases, to look for 'main effects,' not interactions. The interaction term is loosely hooked on to the model, and the idea generally is to try to shake it off. Therefore, upon encountering interactions in the data, investigators frequently attempt to remove them through scale transformations. Sometimes this is effective for ordinal interactions, but never for disordinal cases (Lubin, 1961). If transformations fail, a more drastic solution may be offered by discarding parts of the data. Surprisingly, such procedures can be found in behavior genetics research just as they are in other areas of behavioral studies. Broadhurst (1967, p. 295) has pointed out, for instance, that two important assumptions are involved in biometrical methods of genetic analysis; these are that there be "no interaction between genotype and environment," and that the gene effects "be additive over the range of variations" studied! (Rather startling assumptions to be built into a method designed for use in a science of variations, but, fortunately, Broadhurst and Jinks (1966) have demonstrated that meaningful analyses of gene-environment interactions are possible with the biometrical methods after all.)

Some researchers (cf. Harrington, 1968; Lubin, 1961) argue that when significant interaction effects are turned up in the analysis of variance, the interaction term itself should be considered an important feature of the situation under study. Instead of attempting to eradicate the interaction term statistically, the aforementioned authors suggest that we try to explain it. Lubin (1961), who incidentally was speaking about nonadditive interactions generally rather than gene-environment relationships specifically, has stated the problem succinctly: "To me it's far more important to determine the form of the equation relating the treatment effect to the block (genotype, strain, group) effect than to make accurate statistical inferences about the variance of the difference between two means. If a transformation eliminates the interaction, the inverse of the transformation specifies an equation which is a good fit to the raw data." The first danger of the analysis of variance model and methods stemming from it, then, is that important interaction effects will be looked upon as trivial error variance or will be lost in statistical manoeuvres.

Insert Fig. 1 about here

The second difficulty is that, in analyses that include several different genotypes or several different environmental treatments for comparison, different types of relationships may emerge and may, in some instances, effectively cancel each other. For graphic illustration of a situation in which different kinds of relationships are found, I have plotted in Figure 1 some of the data reported by Henderson (1970b) in a study of early experience effects on mouse behavior. There are 16 possible comparisons between strains. Among these:

a) Disordinal interactions, involving rank order reversals, appear in three comparisons--between BALB and C3H, between C3H and A/J, and between C3H and RF.

b) Most of the interactions are ordinal, with quantitative changes only--BALB versus all strains except C3H, C57BL versus all except C3H, and DBA versus C57BL and C3H.

c) No comparison shows perfect additivity, but that between C57BL and C3H deviates only slightly from an additive relationship with both strains showing nearly identical decreases in time to food goal in the enriched, compared to the standard, environment.

d) One pair of strains gives identical means in both environments and fails to show any difference in behavior associated with the environmental treatments--AJ and RF.

In Henderson's study, a significant interaction effect was obtained in the analysis of variance. Had somewhat more of the strain comparisons shown additive relationships, however, the overall interaction term might have been nonsignificant even though some of the pairs showed markedly different responses to the environmental treatments. In summary, the analysis of variance model can mislead, and the limitation of the meaning of 'interaction' to nonadditive relationships seems unwarranted.

In passing, it may be noted that Haldane (1946), in a now classical paper on the interaction of nature and nurture, included additive relationships among the possible types of significant interactions that may occur between genotypes and environments. The additive relationships, in fact, account for a sizeable proportion of such possibilities. Haldane bequeathed to us a formula, $(mn)!/m!n!$, to describe the number of theoretically possible types of interactions that might be found for m genotypes in n environments if all phenotypes differ from each other (i.e., between all genotypes in all environments). These are, however, theoretical possibilities, whose full, impressive range may rarely be encountered in reality.

The purpose in classifying interactions is, or should be, to allow us to find reasonable ways to interpret mechanisms underlying the interactions. One classification-for-interpretation scheme has been offered by Vale and Vale (1969) who propose that additive and many ordinal interactions indicate that the same process underlies the phenotypic response to the environment in all of the genotypes under study. Disordinal interactions, however, are considered in this scheme to reflect differences in the processes underlying the response in different genotypes. The latter type of finding might occur when comparisons of crudely similar behavior (e.g., maternal behavior) are made between species, when comparisons are made among genetically heterogeneous groups whose phenotypes may be similar in some circumstances but not in others (or between phenocopies and 'hereditary' disorders), when the phenotype being measured is not the same in all groups or all environmental conditions. It should be noted, though, that disordinal interactions may not necessarily imply differences in basic processes; for example, as Henderson (1968) suggests, if the relationship between emotional arousal and amount of prior stimulation should be U-shaped and if two genotypes have different optimal levels of stimulation, and if comparisons are made between only two or a very few levels of stimulation as is usual, then the effects of stimulation may appear opposite in the two genotypes while comparisons at a larger number of treatment levels would show consistency in the relationship between treatments and the effect upon behavior. This point bears repeating: differential thresholds of sensitivity--whether we are concerned with sensory responses or with responses to drugs, alcohol, lack of sleep, etc.--can produce functions that look very different for different individuals over large ranges of intensity levels but, with sufficient extension of these ranges, most individuals may show similar (though widely displaced) treatment-response functions.

The foregoing comments do not detract from Vale and Vale's scheme as a first-approximation working base that may be useful in analyzing and understanding G-E interactions.

Just As the Twig Is Bent? (Illustrations From Early Experience Studies)

From Freud to Spitz and Bowlby right up to our most contemporary literature, it has been taken almost as an article of faith that the effects of experiences in early infancy are profound, enduring, and essentially universal for the members of a species. To a considerable extent, such assumptions are correct. A handful of studies that have looked at genetic effects along with differences in early treatments, however, have some other things to show.

My purpose in discussing this research here is not so much to review the early experience concept as it is to call attention, through a brief scanning of data, to the kinds of consistencies and inconsistencies that are likely to appear when a considerable body of results in gene-environment interactions is at hand. The work on early experience and subsequent behavioral development happens to offer a number of comparisons on some of the same strains, the same phenotypic measures, and the same environmental treatments. Though not intended as an exhaustive coverage of the literature, the collection of fifteen studies referred to in Table 1 represents a good sampling of the available mouse research without selection for results.

Insert Table 1 about here

Most of the studies include more than one measure of behavior; in some instances, the separate measures are supposed to be tapping the same phenotypic trait. We can look first for significant effects of early experience upon the later measures of behavior. We find that out of a total of 39 measures, there are 36 in which at least one of the tested strains fails to display a significant difference between the experimental and control conditions. Looking at all strains x measures, we have a total of 160 opportunities in which to see significant effects of the early treatments. Actually, in 85 of these cases the early experience does not significantly influence performance on the subsequent behavioral test.

Reference to the original studies summarized here would plainly show us that all of the early treatments investigated do have very pronounced effects upon some behaviors in some strains. But the effects are far from universal. In fact, it seems that we have a better than even chance of not finding a significant relationship between an early treatment and a subsequent measure of behavior!

Interaction effects between genotypes and treatments can be examined for 31 behavioral measures on which two or more strains have been tested. In thirteen of these comparisons, the treatment has an opposite influence upon behavior in one or more strains compared to the other strains under study (last column of Table 1). Disordinal interactions (reversals of rank orders between two or more strains from the control to the experimental condition) occur in fourteen out of the 31 comparisons. We can choose to lay stress upon these complicated relationships, or we can decide to emphasize that, in over half of the comparisons, when treatment effects occur, they tend to exhibit fairly regular patterns across genotypes.

Insert Table 2 about here

There is a sufficient number of observations on some of the strains to permit claser examination by strain and type of early experience. Table 2 shows the number of behaviors measured and the number in which experimental and control animals differed significantly, for each of five strains and several types of experimental treatments. It can be seen that the C57BL strain responds to all types of treatments more frequently than do other strains--thus bearing out observations made by Ginsburg (1967), Henderson (1968), and others on the lability of the C57BL group--BALB shows low responsiveness at least to the treatments considered here. The data are too scanty to allow careful comparisons to be made with regard to differential responsitivities to specific treatments in different strains. They suggest, however, that for some of the strains (C57BL, DBA, and C3H) general background variables, such as isolation, environmental enrichment, or cage illumination, may be less critical than more specific, possibly traumatic, events, such as handling, shock, and noxious noise. The opposite seems to be true for BALB, however.

The behavioral measures that are most likely to reflect the influences of treatments also tend to differ among the various strains. For example, in the highly responsive C57BL strain, most of the behavioral measures (see Table 1) are substantially affected by the early experience treatments, but defecation scores are not greatly changed between controls and experimental subjects in most of the studies; C57BL's generally give low open-field defecation scores anyway. C3H, which shows treatment effects in only about 40% of the behavioral measures, seems especially unresponsive where measures involving learning (maze, avoidance or water escape) are concerned, with only two of eight such measures showing an influence of the experimental manipulation. For DBA, on the other hand, maze-learning is the measure showing maximal response to the early treatments (in 5 out of 6 observations). There is a large amount of literature on strain differences in behavior, quite a number of consistencies have been demonstrated in the relative phenotypic performances of several strains compared to each other, and some attempts have been made to construct 'behavioral profiles' describing the relative strengths of various phenotypic characters within the different strains. The findings in the early experience studies tend to be consonant with the more general literature on strain differences. While two strains may frequently reverse rank orders of performance as a result of the treatments applied in infancy, such reversals are generally not found in behaviors on which one or the other of the strains usually scores particularly high or particularly low. G-E interactions frequently appear to be chaotic especially when seen within the confines of a single investigation, but Henderson (1958, p. 150) has noted that "most of these interactions are probably entirely consistent and interpretable when sufficient information is made available through the use of adequate designs and analysis techniques."

Before leaving this section, let me mention that the finding of nonsignificant treatment effects in a sizeable portion of measures of later behavior is by no means confined to mouse research or to early experience studies. Similar observations on manipulations during infancy can be made in studies on rats (cf. Levine and Broadhurst, 1963), and dogs (cf. Fuller, 1963); and there is one intriguing report (Kaufman and Rosenblum, 1967) on the effects of separation from mothers in pigtail monkeys (Macaca nemestrina), in which the offspring of the dominant female failed to show the characteristic depression displayed by the other infants--a possible genotype-environment interaction? Work on prenatal or preconception stimulation and on foster-rearing frequently also shows that one or more strains are not affected by the treatment (cf. DeFries et al., 1967; Resler, 1963; Thompson and Olian, 1961).

Parameters of Interaction

What are we measuring? when? in what circumstances? in whom? These are the questions that we are asking when we talk about gene-environment interactions. The question of genotype is, of course, basic to the discussion throughout this paper and need not be dealt with specifically here. The questions of behavioral phenotypes, time, and environmental conditions have, fortunately, received considerable attention from many other authors, so that I need only make a very few remarks about some points that seem, to me, most pertinent to the study of interactions.

Behavioral phenotypes. Two questions arise about the choice of behavioral phenotypes for investigation. First, are we really measuring what we think we are studying or are we measuring 'noise' from interfering responses? If we want to compare learning processes in two groups or in two different environments, are we getting at the same phenotypic levels in both groups, both environments? If we are comparing learning in two groups and two environments, is our measure uncontaminated with competing behaviors in all four cells (or, at least, is the type and amount of contamination constant over cells)? There are numerous illustrations in which apparent strain differences in learning, activity levels, social behaviors, memory, emotionality, etc., have turned out to be based in differences in, for instance, fearfulness or the motivational aspects of the task in the circumstances peculiar to the testing situation (cf. Fuller, 1967; Henderson, 1968; Ross et al., 1966). Obviously, this is an especially serious problem in research on human behaviors where testing conditions may tap different functions in different subjects or groups of subjects (e.g., schizophrenics versus nonschizophrenics).

The second problem has to do with the relevance of our behavioral measures to the organisms under study. Consider, for example, the study in which the customary rat-type measure of emotionality, i.e., open-field defecation, was applied to cats; felus domesticus, having a very different response style, supplies no data in this situation, as could have been predicted by anyone who knew the animal. Whitney (1970) among others, has recently discussed the arbitrary nature of the operational definitions assigned to many of our traditional laboratory measures and the dangers of drawing analogies between species based on superficial resemblances in behavioral variables.

Discussions of these and other problems relating to the choice and interpretation of behavioral phenotypes may be found in Ginsburg (1967) and Thompson (1967).

Time. A good deal of attention has been given to critical periods when events must occur if a particular response (behavioral or physiological) is to develop and to sensitive periods when the organism is maximally vulnerable to specific types of treatments. We know of a great many behaviors for which different genotypes show different sensitive periods, outstanding examples being those found in audiogenic seizure research (cf. Fuller and Collins, 1970). Fuller and Collins point out that there even genotypic differences in the diurnal rhythm of susceptibility to seizures. One point often not mentioned in discussions of sensitive periods is that such periods need not be confined to a single interval of time in the life span. Many disease susceptibilities, for example, appear to show periods of heightened vulnerability occurring at several different times over the lifespan.

Some seeming. dissimilarity among different sets of gene-environment interactions disappears when time factors and development rates are taken into account (cf. Henderson, 1968). But sometimes the opposite is true, and we find discrepancies emerging only when observations are taken at different points in time. Fuller and Clark (1968) have shown that the time elapsed between an environmental treatment and the measurement of behavior can be an important variable. Similarities in responses observed shortly after the application of a particular treatment may diverge with time, as individual differences in recovery or retention rates gradually take over.

Environment As mentioned earlier in this discussion, it is especially critical in attempting to understand gene-environment interactions to specify the range of stimulus intensities examined and to consider the possibility that extensions of that range may show us regularities in the response functions of different genotypes which are obscured when measures are taken in a more restricted range.

There is one final point to be mentioned here about the choice of environmental treatments to be examined in meaningful analyses of behavior and genetic variable. This point is closely tied to one made above about the selection of behaviors that are relevant to the organism under study. It is simply that we must also question the meaning of environmental conditions imposed experimentally or seen in field observations in terms of evolutionary history. It has been pointed out many times that a good deal of work in the behavioral sciences is as flawed by the neglect of the kinds of environments that the subject species may be expected to encounter naturally as it is marred by inadequacies in the choice of behavioral phenotypes for study.

Man is a special problem. What shall we say is man's 'natural' environment? From what baseline can we speak of deprivation, enrichment or inadequacy of stimulation during infancy and early childhood? We may not have answers to these questions, especially when we reckon with the fact that man is a genetically diverse animal adapted to many different environments. Nevertheless, I would quarrel with those who claim that no environments are universally good or bad. Surely a vermin-infested slum is a bad environment for any child, though there may be some environments that are relatively worse and some genotypes that manage relatively better than others in the same bad surroundings.

Concluding Remarks

Not so very long ago, most of the theoretical positions subsumed by the behavioral sciences found at least one common meeting ground: genetics could be safely ignored because heredity had little, if anything, to do with behavior. Environment was counted the all-important force in behavioral development--though the bond of unity among theorists quickly dissolved when it came to specifying what the significant aspects of environment might be.

Nowadays, the nature-nurture controversy is often declared to be a thing of the past. "Everyone," says David Rosenthal (1968, p. 78), "agrees that all human behavior is a function of both heredity and environment..." Perhaps everyone does not agree, for the same volume in which Rosenthal's enthusiastic note is sounded also contains a more skeptical point of view: "I would emphasize...the relative lack of scientific information concerning the genetic basis for human behavior" (Haller, 1968, p. 225). But if refusals to credit geneticists with having compellingly demonstrated their claims do persist, at least it may be said that outright refusals to credit genetic factors with any influence on behavior appear in the psychological and psychiatric literature with increasing rarity. Indeed, it is more and more common for contemporary discussions of both animal and human behavior to include some reference to interactions between genes and environment. Moreover, in recent years several leading proponents of behavioral theories heretofore conspicuously lacking in attention to any biological differences among individuals have seen fit to take notice of genetic factors, declaring further that they themselves had long held interactionist views about behavior! (These were evidently very privately held views that were strictly guarded against in the serious businesses of research and theory-making.)

All of these should be encouraging signs. Yet paper tributes to the contributions of genes can scarcely be said to point to a revolution in the established environmentalist traditions that have so long dominated the behavioral fields. Nor do they indicate accommodation. It is only necessary to observe that, when they occur, acknowledgments of heritable effects are usually tucked into the general introductory remarks or the closing caveats of an article to realize that the implications of genotypic diversity have penetrated neither thinking nor action levels in behavioral studies. Admitting or not that heredity does have something to do with behavior after all, most students of behavior continue in the comfortable assumption that genetic principles and methods can still be largely ignored.

Dobzhansky (1962) and others have cited a variety of explanations for the emergence in former years of an anti-hereditarian bias. These ranged from historical reasons rooted in some of the earliest philosophical heritage of the social sciences, to the perversions of social Darwinism and its noxious offshoots, to misapprehensions about 'curability' and inevitability, to emotional responses having to do with one's own self-determination. All of these background ideas were alike, of course, in that they represented statements of basic ignorance about G-E interactions. All posed alternatives: either genetic fixity, with phenotypic expression being insusceptible to change in response to environmental factors, or limitless environmental plasticity, with heredity being inconsequential in the development of behavior.

That state of confusion seems to be chronic, for when we examine many of the modern treatments of nature and nurture we are likely to find them retaining the notion of opposed forces, teams that rarely go into play simultaneously. Thus, we find that environment is said to operate "irrespective of genetic constitution," "in spite of genetic limitations," or "without regard to heredity." Quite often, references to the interaction of heredity and environment turn out to mean nothing more than "there must be a genotype, i.e., organism, upon which environment can act." Lacking is an appreciation of the enormous amount of genetic variability existing in human and animal populations and the individuality of the reaction-ranges (Gottesman, 1968) of each of these variants. In short, the very essence of the gene-environment interaction concept has been missed. The nature-nurture controversy has not really died or even faded away; with a sprinkling of a few pleasant words about heredity for modern flavor, the nurture side of the argument thrives in quiet complacency.

To a large extent, developments in behavior genetics have not been conducive to dispelling the confusion. As noted earlier in this paper, there have been comparatively few attempts to take up the challenges of exploration and explanation in connection with G-E interactions and behavior. Part of this neglect can be accounted for by the fact that behavior geneticists, as a group, have often kept busy just in the effort to gain from entrenched environmentalists some enduring recognition of the need to reckon with heredity in behavioral studies. Unfortunately also, discussions of the implications of genetics for behavior sometimes convey the impression that endlessly proliferating interactions between hereditary and environmental variations can only result in a morass of disorderly individual differences. That is a discouraging prospect and one which is certainly overdrawn! Students of behavior may well fail to see any possibilities of discovering meanings in the chaotic state implied. With work on plants and lower organisms and with examples from developmental embryology as a frame of reference, workers in behavior genetics, however, should be able to think of gene-environment relationships in terms of underlying mechanisms in which some order is to be found.

I have tried to demonstrate in the data from the early experience literature examined briefly here that G-E interactions are numerous and that treatment effects are frequently reversed in direction for different genotypes. At the same time, I have tried to emphasize that not every strain X treatment combination produces a discernible difference in behavior compared to (a) the untreated members of the same strain or (b) similarly treated members of a different strain. Thus, environmental treatments very often do not produce any effect in some genotypes--at least not any change in the behaviors studied--strains sometimes do not differ among themselves, and, when they do differ, they more often show quantitative deviations from each other than sign reversals in performance. Moreover, it is possible to see some, admittedly crude, patterns of responsivity among some of the strains included in the several studies reviewed here. Thiessen (1965) and Abeelen (1966) have called attention to the consistencies in relative performances of several mouse strains when studied in a number of investigations on various behavioral measures that presumably tap a common phenotypic domain. Ginsburg (1967) and others have commented upon the further finding that some strains (e.g., the C57BL types) are consistently more labile, more responsive to (at least certain kinds of) treatments than other strains. The data from the early experience studies tend to show both performance level and responsitivity consistencies across strains, as well as consistencies in the behavioral phenotypes which do and do not maximally reflect treatment effects within each strain. Diversity in plenty is certainly there, but, as Henderson (1968) and Vale and Vale (1969) have stressed, basic regularities can be found among the various sets of interactions with sufficiently fine-grained analysis, and sometimes even with a very coarse net such as that employed here.

Genotypic uniqueness is a fact (Hirsch, 1962). So, too, probably, is the uniqueness of total environmental complexes encountered by each individual. Nevertheless, it may be reasonable to suppose that many genotypic-environmental encounters do not produce interactions so unique that they differ appreciably from interactions formed in the encounters of many other genotypes and environments. Data reported by Broadhurst and Jinks (1966), for instance, strongly suggest that stability of behavioral development is under genetic control and that the genes which confer greater stability, i.e., resistance to environmentally induced variations, tend to show dominance. Their discussion of the evolutionary significance of such behavioral stability during development proposes that gross individual differences in adult reactions to stimuli might be highly disadvantageous in many natural populations. Early stability, it is further suggested, might thus afford a comparatively homogeneous baseline of adult reactivity, from which a considerable amount of behavioral plasticity could then emerge. The hypothesis is of interest in that it offers a possible explanation for the fact that interactions between genotypes and environments do not seem to represent quite so much buzzing confusion as their separate diversities might indicate.

The idea of limits to the amount of phenotypic variation attained through G-E interactions has bëen stated most lucidly by Vale and Vale (1969). They say: "If the cnalization concept may be applied to behaviors, there would appear to be a property of development that acts to reduce the phenotypic expression of behavioral uniqueness. This balance is necessary if a population is to exploit a limited species range while maintaining the genetic diversity imperative for evolution. If every genetic and every environmental difference produced important phenotypic differences, it is difficult to see how any population could reproduce and survive, so morphologically, biochemically and behaviorally different would the individuals composing it be. In fact, it has been observed (e.g., Dobzhansky, 1955; Lerner, 1954, p. 6) that morphological variance in natural populations is smaller than would be expected considering genetic segregation and differences in environment."

The point has been made by Vale and Vale (1969) that the interactions of nature and nurture are often to be understood in terms of basic mechanisms underlying the shared behavioral response. Ginsburg (1967) has also stressed the usefulness of analyzing G-E interactions as a lever for the "meaningful investigation of problems of behavior at every level, from the molecular, through the organismic, to the population" (p. 153). In other areas of genetics, interactions are used, for example, to explore the timing and mechanisms involved in the development of specific characters (Caspari, 1964), to investigate maternal-fetal responses influencing developmental patterns, and to explore the action of specific environmental agents upon metabolic pathways (Fraser, 1963). And Harris (1970), in a quite different context, has commented that one of the important applications of research in human genetics will lie in the possibilities of modifying or tailoring the environment according to the individual needs of persons with different genetic constitutions. In short, rather than regarding heredity-environment interactions as nuisance variables, many people are looking for ways to take advantage of them as a type of research stratagem.

Schizophrenia is a case in point where closer attention to gene-environment interactions should be a minimal requirement for all future research designs. If most of us who pursue the etiological ignes fatui of schizophrenia really believe that some kind of interactional phenomenon is involved (cf. Rosenthal and Kety, 1968, entire proceedings, The Transmission of Schizophrenia) then why are we so often found to be following our separate tracks, nature or nurture, as of old? In choosing to concentrate on one side or the other, we have options of sampling and design that would permit us to include at least gross analyses of G-E interactions. Some progress toward an interactional approach to schizophrenia has already begun to appear with Heston's (1966) study of adoption in children of schizophrenic mothers and the prompt follow-up by other investigators (Kety, Rosenthal, Wender) in making use of adoptee samples (see review of these studies in Rosenthal, 1971). In another elegant attack upon the heredity-environment problem, Rosenthal (1971) and colleagues are comparing children of schizophrenic parents reared in kibbutzim and in their own homes with control children in both types of rearing situations.

In all of these studies, the idea is to separate genetic from rearing variables, the biological transmission of genes from the possible intrafamilial transmission of psychopathology. Clearly, future work will have to take into account subtler aspects of the environment (because, as Heston's work has demonstrated, the proportion of predisposed children manifesting schizophrenia is the same whether they are reared by their schizophrenic parents or by others), but a pattern for the dissection of interactions has now been set by these investigations. Other types of programs which concentrate on the prospective study of individuals presumed to be at risk for the later manifestation of schizophrenia (cf. Anthony, 1968; Erlenmeyer-Kimling, 1968; Mednick & Schulsinger, 1968) may be in a position to examine interactions between genotypes and environmental stresses over various periods of development. In such studies it may be possible, moreover, to use observed interactions to test specific hypotheses about, for example, neurophysiological or biochemical pathways in which aberrations occur.

No studies of gene-environment interactions are going to be easy to do, and the methodological problems, especially in connection with human behavior, are obviously immense. The study of behavior, however, has not been at all well-served thus far by apartheid tactics between environmentalists and geneticists. Rather than ignoring gene-environment interaction or being over-awed by them, we will have to cope with them and learn to put them to our service in the understanding of the 'hows' of behavior.

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Table 1 Generality of strain x treatment effects in some early experience studies in mice

Ref.[1]	Type of experience[2]	Behavioral measures[2]	Strains[3]	Treatment effects	
				Not found[4]	Different directions[5]
(1)	variations in social vs. isolation rearing	1) fighting latency	C5, B	B	---
		2) sexual behavior	C5	C5	---
(2)	handling vs. nonhandling	1) alley crossing	P.m.b., P.m.g.	P.m.g.	yes
		2) activity time		P.m.g.	no
		3) avoidance conditioning		P.m.b.	yes
(3)	infantile trauma (noise)	1) 30-day o.f., defecation, mean	C5, C3, D, J	C5, D, J	no
		2) 30-day o.f., defecation, day 10		D, J	no
		3) stove pipe emergence, time		D	C5
		4) 100-day o.f., defecation, mean		C5	no
		5) 100-day o.f., motility, mean		C3, D	D
(4)	handling vs. nonhandling	1) fighting latency	C5, D	---	yes
(5)	infantile trauma (noise)	1) 30-day o.f., defecation	C5, C3, D, J	C3, J	no
		2) 30-day o.f., motility		D, J	?
		3) stove pipe emergence, time		D, (J ?)	no
		4) 100-day o.f., defecation		all	?
		5) 100-day o.f., motility		J	C5
(6)	infantile trauma (noise)	1) maze errors	C3, D, A/A	C3	no
		2) maze, time (g), mean		A/A	A/A
		3) maze, time (g), day 13-15		C3	no
		4) maze, time (f), mean		all	no
		5) maze, time (f), day 13-15		C3	no
		6) water escape, time, trend		all	D

Table 1 - p. 2

Ref.[1]	Type of experience[2]	Behavioral measures[2]	Strains[3]	Treatment effects: Not found[4]	Treatment effects: Different directions[5]
(7)	infantile trauma (noise)	1) maze, errors	(C3, D, A/A and three F_1 hybrids*)	Three F_1 hybrids	no
		2) water escape, time		all	no
(8)	shock vs. handling vs. nonhandling	1) defecation, o.f.	C5	---	---
		2) avoidance conditioning		---	---
(8a)	shock vs. handling vs. nonhandling	1) activity, o.f.	B	B	---
		2) defecation, o.f.		B	---
		3) runway emergence		B	---
		4) avoidance conditioning		B	---
(9)	handling vs. nonhandling	1) fighting latency	C5, C3, C-A	C3, C-A	no
(10)	shock vs. handling vs. nonhandling	1) activity, o.f.	(C5, B, C3, D, & twelve F_1 hybrids)	C3, B, four $C3F_1$, three BF_1	no
		2) defecation, o.f.		C5, C3, three $C3F_1$, BDF_1	B
(11)	high vs. low illumination	1) defecation, o.f.	C5, B	C5, B	yes
		2) activity, o.f.		C5	yes
		(* tested in high vs. low illumination; B's activity higher in low illumination testing.)			
(12)	enriched vs. standard cages	1) hoarding	C3, J	C3	no
(13)	daily dosages CPZ vs. AMPH vs. saline	1) dominance	(random-bred Swiss, P.m.b.)	P.m.b.	no

Table 1 - p. 3

Ref.[1]	Type of experience[2]	Behavioral measures[2]	Strains[3]	Treatment effects	
				Not found	Different directions[5]
(14)	enriched vs. standard cages	1) spontaneous alteration	(C5, B, C3, D, A/J, RF, and six F_1 hybrid averages*)	all inbred, all F_1 except DF_1	C5, D, $C3F_1$, DF_1, RFF_1 vs. all others
(15)	enriched vs. standard cages	1) food-seeking (problem-solving)	(C5, B, C3, D, A/J, RF & twelve F_1 hybrid averages)	D, A/J, RF_1, one A/JF_1, one RFF_1	F_1 of A/J female vs. all others

Notes:

[1] References (in order)--(1) King, 1957; (2) King & Eleftheriou, 1959; (3) Lindzey et al., 1960; (4) Ginsburg, 1963; (5) Lindzey et al., 1963; (6 & 7) Winston, 1963, 1964; (8 & 8a) Henderson, 1964, 1967a; (9) Ginsburg, 1967; (10) Henderson, 1967b; (11) Dixon & DeFries, 1968; (12) Manosevitz et al., 1968; (13) Wolf & Rowland, 1969; (14 & 15) Henderson, 1970a, 1970b.

[2] Abbreviations (in cols. 2 & 3)--o.f. = open field test; maze, time (g) = time to reach goal; maze time (f) = time from final choice to food cup; CPZ = chlorpromazine; AMPH = amphetamine.

[3] Strains--C5 = C57BL; B = BALB; P.m.b. = Peromyscus maniculatus bairdii; P.m.g. = Peromyscus maniculatus gracilis; C3 = C3H; D = DBA; J = JK; A/A = A/Alb; F_1's = hybrid generation crosses between the various inbred strains under study; C-A = C(Bagg) albino.

* indicates no reciprocal cross data for F_1 hybrids.

[4] Not found (col. 5)--Experience effect not significant for the strain(s) shown.

[5] Different direction--yes = opposite effects of experience in the 2 strains studied; no = same directional effects of experience in the 2 or more strains studied; strain symbol(s) = opposite effects in the indicated strain(s) compared to other strains under study.

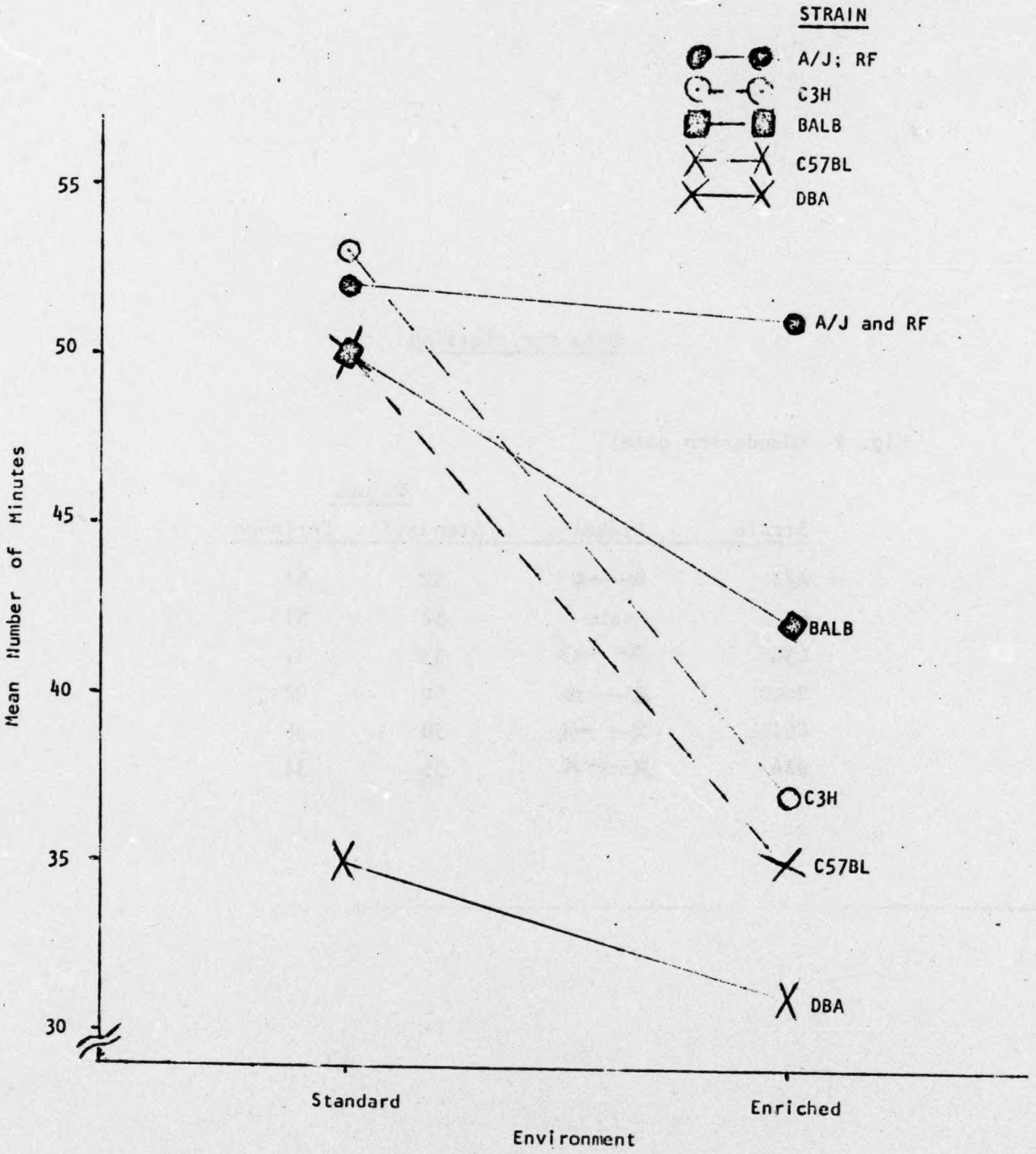
Table 2 Types of early experience treatments: number of significant effects upon behavioral observations for several inbred mouse strains.

Type of experience	C57Bl		BALB		C3H		DBA		JK	
	obs.	sig.	obs.	sig.	obs.	sig.	obs.	sig.	obs.	sig.
Social-isolation,	2	1	1	0	-	-	-	-	-	-
enriched-standard	2	1	2	1	3	1	2	0	1	1
Subtotal	4	2	3	1	3	1	2	0	1	1
Handling,	2	2	-	-	1	0	1	1	-	-
handling-shock,	4	3	6	1	2	2	2	2	0	0
infantile trauma (noise)	10	7	-	-	18	8	18	9	10	4
Subtotal	16	12	6	1	21	10	21	12	10	4
Other (light)	2	0	2	1	-	-	-	-	-	-
All	22	14	11	3	24	10	23	12	11	5

Note: [1]Strains--above strains selected from studies in Table based on frequency of observations.

Caption

Fig. 1. Illustrative data from Henderson (1970b, Table 1) showing mean number of minutes required to reach food for 6 inbred strains of mice reared in standard and enriched environments.


STRAIN
A/J; RF
C3H
BALB
C57BL
DBA
55
50
45
40
35
30
Mean Number of Minutes
A/J and RF
BALB
C3H
C57BL
DBA
Standard
Enriched
Environment

Data for plotting

Fig. 1 (Henderson data)

		Values	
Strain	Symbol	Standard	Enriched
A/J	●—●	52	51
RF	same	52	51
C3H	○- -○	53	37
BALB	▲—▲	50	42
C57BL	×- -×	50	35
DBA	×—×	35	31

QUANTITATIVE ASPECTS OF GENETICS AND ENVIRONMENT IN THE DETERMINATION OF BEHAVIOR

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Quantitative Aspects of Genetics and Environment in the Determination of Behavior

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In spite of the remarkable advances which have occurred within molecular genetics, the practical problem of dealing with polygenic characters is still with us. In fact, recognition that the most interesting human characters such as intelligence, temperament, and physical structure are probably highly polygenic has recently led to a reappraisal of projections for genetic intervention in man (Davis, 1970).

Quantitative genetic theory was developed by applied scientists faced with the practical problem of improving polygenic characters in domestic animals and plants. Although this theory has not been substantially altered within the last several decades, its utilitarian value remains. Thus, it seems likely that such concepts as heritability, genetic correlation, selection index, etc. will be indispensible when the issue of qualitative population control is finally faced. However, since quantitative genetics was largely developed for application to animal and plant breeding, it is not surprising that its concepts and methods are not immediately applicable to important social issues such as the heritable nature of racial differences or the feasibility of modifying behavior by environmental means. The primary objective of this paper is to illustrate how the concepts of quantitative genetics might be extended to deal with such problems.

The Heritable Nature of Group Differences

Jensen (1969) has recently marshalled compelling evidence to demonstrate that intelligence, as measured by conventional IQ tests, is a highly heritable character within Caucasian populations. From this evidence, Jensen hypothesized that genetic factors are strongly implicated in the reported difference of 15 IQ points between the means of Caucasians and Afro-Americans. In a critique of Jensen's paper, Lewontin (1970) showed that the genetical basis of inter-racial differences is not a simple function of the within-group heritability; however, the actual functional relationship between these variables was not explored. In view of the obvious importance of this issue, an examination of the relationship between within-group heritability and the heritable nature of group differences is clearly in order.

Heritability

The concept of heritability has been discussed lucidly by both Jensen (1969) and Lewontin (1970); thus, only a relatively brief review of this concept will be presented here. In quantitative genetic theory (Falconer, 1960), the measured value of some character of an individual, i.e., its phenotypic value, is assumed to be some function of its genotype and the environment in which it develops. For simplicity, we may assume the following linear mathematical model:

$$P = G + E, \tag{1}$$

where P is the phenotypic value, G is the genotypic value, i.e., the value conferred upon the individual by its genotype, and E is a deviation caused by the environment. Thus, since the mean environmental deviation is zero, the mean phenotypic value would estimate G in a population of like genotypes.

If non-linear interactions occur between G and E, another term should be included in equation 1. A method for assessing the importance of such genotype-environment interactions from human twin data has recently been suggested by Jinks and Fulker (1970). If such interactions are found to be important in a set of data, but are not of special interest to the investigator, the raw data may be subjected to a scalar transformation which may render the original simple model appropriate.

From equation 1, it may be seen that the phenotypic variance may be simply expressed as follows:

$$V_P = V_G + V_E, \qquad (2)$$

where V_P is the phenotypic variance, V_G is the genotypic variance, and V_E is the environmental variance. If a correlation exists between G and E, the assumptions underlying the simple model (equation 1) are not violated; however, equation 2 should then contain a term corresponding to twice the covariance of G and E. Roberts (1967) has suggested an intriguing solution to this problem. He suggests that the environment should be defined as affecting the phenotype independently of the genotype. Thus, if the genotype of an individual influences its choice of environment, this effect should be considered to be genetic, even if it is mediated by such things as habitat selection.

The genotypic variance may also be partitioned into components due to different causes. The gene, not the genotype, is the unit of transmission. Therefore, the resemblance of relatives is due chiefly to the average effects of genes. In principle, each allele has an average effect for a character measured on individuals in a population. When summed, these average effects result in an expected or additive genetic value. Dominance and epistasis, however, may cause the genotypic value to deviate from this value. Symbolically,

$$G = A + D + I, \tag{3}$$

where G is the genotypic value, A is the additive genetic value (sum of the average effect of the alleles across all loci), D is the dominance deviation (non-linear interaction between alleles at the same locus, summed across all loci), and I is the epistatic interaction (non-linear interaction between alleles at different loci). A, D and I are all independent; thus,

$$V_G = V_A + V_D + V_I, \tag{4}$$

where V_A is the additive genetic variance, V_D is the dominance variance, and V_I is the epistatic variance. (See Lush, 1948, and Falconer, 1960, for a more detailed discussion of the principles underlying the partitioning of genotypic variance.)

The ratio of the additive genetic variance to the phenotypic variance is known as heritability in the narrow sense (Lush, 1949) or simply heritability (Falconer, 1960). The proportion of the phenotypic variance due to both additive and non-additive genetic variance is referred to as heritability in the broad sense (Lush, 1949). Heritability (narrow sense) has both descriptive and predictive properties. In addition to indicating the proportion of the variance due to the average effects of genes in a population, it may also be shown that heritability is equivalent to the regression of the additive genetic value of an individual on its phenotypic value. Thus, heritability may be used to predict the additive genetic value of an individual and the change in a population due to various breeding systems (Falconer, 1960).

For this reason, heritability in its narrow sense should be of particular importance to those purportedly interested in eugenic considerations.

Because of the predictive property of heritability, it is important to not adjust the estimate for lack of perfect test reliability. Such adjustment may be reasonable when one wishes to compare estimates obtained from data in which tests with different reliabilities have been used. However, in such a case, the resulting estimates no longer correspond directly to heritability based upon single records. Instead, the estimates correspond to the heritability of the average of N records on each individual, where N is equal to infinity. The heritability of the average of N records ($h^2_{\bar{P}}$) is as follows:

$$h^2_{\bar{P}} = \frac{Nh^2}{1 + (N - 1)t}, \qquad (5)$$

where N is the number of records on an individual, h^2 is the heritability based upon single records (not adjusted for test reliability), and t is the correlation between repeated records on the same individuals. It may be shown that $h^2_{\bar{P}}$ is equivalent to the regression of the additive genetic value of an individual on the mean of N records on that individual.

The various methods of estimating heritability will not be discussed here. These procedures, as well as some of the special problems encountered with human data, have been discussed previously by the author (DeFries, 1967).

Within-Group Heritability and the Heritability of the Group Average

When a population is composed of two or more groups, the genetic and phenotypic variances in the population may each be partitioned into two parts: that between groups and that within groups. The ratio of the additive genetic variance within groups to the phenotypic variance within groups yields the within-group heritability (h_w^2):

$$h_w^2 = h^2 \frac{(1 - r)}{(1 - t)}, \qquad (6)$$

where h^2 is the population heritability (narrow sense, not adjusted for test reliability), t is the phenotypic correlation (intra-class) among members of the same group, and r is the analogous genetic correlation, i.e., the correlation of the additive genetic values of members of the same group. For groups composed of close relatives, r is equal to the coefficient of relationship. However, for groups which have been isolated for many generations, selection and/or genetic drift could change gene frequencies in the groups such that r may differ considerably from the coefficient of relationship. It may be shown that h_w^2 is equivalent to the regression of the additive genetic value of an individual on its observed phenotypic value, where the phenotypic value is expressed as a deviation from the group mean.

The ratio of the additive genetic variance between groups to the phenotypic variance between groups yields the heritability of the group average (h_f^2):

$$h_f^2 = h^2 \left[\frac{1 + (n - 1)r}{1 + (n - 1)t}\right], \qquad (7)$$

where n is the number of individuals measured within the group under consideration, and h^2, r and t are defined as above. It may be shown that h_f^2 is equivalent to the regression of the mean additive genetic value of a group on its mean phenotypic value, expressed as a deviation from the grand mean; thus, h_f^2 may be used to estimate the mean additive genetic value of a group or to explore the heritable nature of group differences. (The symbols and expressions of h_w^2 and h_f^2 are those used by Falconer, 1960, in his discussion of the heritability of within-family deviations and family means, respectively.)

From the above expression it is obvious that h_f^2 is a function of h_w^2 as follows:

$$h_f^2 = h_w^2 \frac{(1 - t)}{(1 - r)} \left[\frac{1 + (n - 1)r}{1 + (n - 1)t}\right] . \qquad (8)$$

When the number of individuals measured within a group is large, h_f^2 reduces to the following approximation:

$$h_f^2 \cong h_w^2 \frac{(1 - t)r}{(1 - r)t} . \qquad (9)$$

When environmental effects are distributed at random across groups, i.e., when environmental deviations of members of the same group are uncorrelated, $t = h^2 r = h_w^2 \frac{(1 - t)r}{(1 - r)}$. Upon substitution of this expression for t into the denominator of equation 9, it may be seen that h_f^2 will equal one when h_w^2 is non-zero and when environmental effects are distributed at random. t is a function of h^2, r, and the environmental correlation of members of the group. It may thus be shown that the maximum value that r may achieve is given by $\frac{t}{h^2} = \frac{t(1 - r)}{h_w^2 (1 - t)}$, at which point h_f^2 is equal to one. Thus, although r may exceed t, the maximum value of r is limited by the size of h^2 and t.

Equation 9 clarifies the two troubling cases raised by Lewontin (1970) which suggested that the heritability of the group average (or the heritable nature of group differences) bore no logical relation to the within-group heritability. In his first case, two completely inbred lines were reared in similar environments. Although the difference between lines is thus entirely due to gene effects, h_w^2 in isogenic lines is zero. From equation 9 it may be seen that h_f^2 is not zero in this case; it is undefined. r will equal one with completely inbred lines.

In Lewontin's second case, two random samples from an open-pollinated variety (or genetically heterogeneous population) are reared in quite different environments. In this case, h_w^2 is non-zero, yet all the difference observed between groups should be environmental. If the random samples are sufficiently large that genetic equality between the two groups is ensured, r will approach zero, but t will be non-zero; thus, as seen from equation 9, h_f^2 will approach zero in this case.

Equation 9 may also be used to explore the heritable nature of racial differences in IQ. The value of h_w^2 suggested by Jensen (about 0.8) is almost certainly an overestimate of heritability in the narrow sense. Since it is largely based upon twin comparisons, it will include non-additive genetic variance and possibly some variance due to common environmental effects. In addition, it is based upon correlations which have been adjusted for test reliability and thus is an overestimate of h_w^2 based upon single records. Of course, data from members of the Afro-American group are also necessary to obtain a valid estimate of h_w^2. Because of the uncertainty inherent in the estimate of h_w^2, three possible values will be considered: 0.4; 0.6 and 0.8.

From the reported difference in average IQ between the two groups (15 points) and the standard deviation within (also assumed to be 15 points), it is possible to obtain an estimate of t. Assuming that the group means are known with exactness so that two degrees of freedom are associated with the between-group sum of squares, an estimate of t = 0.20 is obtained.

Unfortunately, no valid estimate of r is available. In his genetic analysis of morbidity data obtained from the major racial groups of Hawaii, Morton (1967) estimated that the inbreeding coefficient was 0.0009 for major races. With low levels of inbreeding, r is approximately twice the coefficient of inbreeding; thus, for morbidity data, r may be as low as 0.002. However, it seems likely that such data from the major races of Hawaii are not at all comparable to IQ data from mainland Afro-Americans and Caucasians.

Various possible values of h_f^2 are tabulated in Table 1 as a function of h_w^2 and r. In these calculations, it was assumed that t = 0.20. Dashed lines in the second and third rows indicate that the maximum value of r must be less than 0.3 when t = 0.20 and h_w^2 = 0.6 or 0.8.

From Table 1 it may be seen that if r were as low as 0.002 (corresponding to that with morbidity data in Hawaii) and if h_w^2 were about 0.6, h_f^2 would be approximately equal to 0.005. If this were the case, of the reported 15 point IQ difference between Afro-Americans and Caucasians, less than 0.1 IQ point would be heritable. However, since no valid estimate of r exists for IQ data, it is impossible to choose a particular value of h_f^2 at this time. Nevertheless, it is abundantly clear from Table 1 that a high within-racial heritability by no means implies a highly heritable racial difference.

Quantitative Aspects of Environmental Determination

As indicated previously, in quantitative genetic theory the genotype is assumed to confer a certain value on an individual, whereas the environment causes a deviation from this value in one direction or the other. Environmental variance is thus a source of error which the experimenter attempts to minimize. Although the principles and techniques of quantitative genetics are directly applicable to the study of behavioral characters in laboratory and domestic animals, some modification of the usual quantitative genetic model may be useful for human behavioral genetics.

Unlike the researcher who studies behavior in laboratory animals, the human behavioral geneticist has little or no direct control over the environment in which his subjects develop. As a consequence, variance in human behavioral characters due to non-genetic causes is not simply a manifestation of random error. On the contrary, some portion of this variance is due to measurable environmental effects which in principle are controllable. Of course, a portion of this environmental variance is caused by uncontrollable factors such as errors of measurement or other intangible effects.

The relative importance of controllable environmental factors or the proportion of the variance in human behavioral characters due to measured environmental effects is of both theoretical and practical interest. The objective of this section is to present an extended model and to consider some possible applications.

Theory

The following is a simple extension of the usual quantitative genetic model:

$$P = G + C + E, \qquad (10)$$

where P is the phenotypic value of an individual, G is the genotypic value, C is the "environmental value," due to measured environmental effects, and E is a positive or negative deviation caused by unmeasured, non-genetic factors. In principle, if the system were completely understood, all environmental effects would contribute to C; thus, the distinction between C and E is a function of the state of knowledge which exists at any given time. When G, C and E are uncorrelated and when no genotype-environmental interactions exist, the phenotypic variance (V_P) may thus be partitioned as follows:

$$V_P = V_G + V_C + V_E . \qquad (11)$$

The extended model permits the formulation of a new population parameter, analogous to heritability, with both descriptive and predictive properties. Let,

$$c^2 = V_C/V_P , \qquad (12)$$

where c^2 is the "coefficient of environmental determination" and represents the proportion of the total variance due to measured environmental effects. c^2 is predictive since it is equivalent to the regression of the environmental value on the phenotypic value. The covariance of the environmental value and the phenotypic value, Cov (CP), is as follows:

$$\text{Cov (CP)} = \text{Cov (C) (G + C + E)} = \text{Cov (CG)} + \text{Cov (CC)} + \text{Cov (CE)}. \qquad (13)$$

When G, C and E are uncorrelated, Cov (CG) = Cov (CE) = 0. Thus, Cov (CP) = Cov (CC) = V_C, i.e., the covariance of C and P is equal to the variance due to C. The regression of C on P, b_{CP}, is as follows:

$$b_{CP} = \frac{\text{Cov (CP)}}{V_P} = \frac{V_C}{V_P} = c^2 ; \qquad (14)$$

thus, the regression of the environmental value on the phenotypic value is equivalent to the coefficient of environmental determination.

In addition, the correlation between C and P, r_{CP}, is equal to the square root of the coefficient of environmental determination:

$$r_{CP} = b_{CP} \frac{\sigma_P}{\sigma_C} = c^2 \frac{1}{c} = c \ . \qquad (15)$$

Application

Since $c^2 = b_{CP}$, the phenotypic value may be used as an index of the environment in which an individual developed. The expected environmental value ($\hat{C}$) may be estimated as follows:

$$\hat{C} = b_{CP} \ (P) = c^2 \ (P) \ , \qquad (16)$$

where P is the phenotypic value of an individual expressed as a deviation from the population mean.

The mean phenotypic value of individuals from an unmeasured population may be estimated from the properties of the normal distribution. The mean phenotypic value of individuals in a truncated portion of the normal curve should deviate from the population mean by (z/p) σ_P units, where z is the height of the ordinate at the point of truncation of the normal curve, p is the proportion of the population in the truncated portion, and σ_P is the phenotypic standard deviation. Values of z for corresponding values of p may be found in various statistical tables (see Fisher and Yates, 1963, Tables II and II.1). For example, let us assume that an intelligence test is administered to a large, normally distributed population. The mean IQ score (phenotypic value) of individuals in the upper 0.01% of the population should be (z/p) σ_P = (.0004/.0001) (15) = 60 IQ points above the population mean. Three major factors are responsible for the scores of these individuals: (1) their heredity, (2) measured environmental effects, and (3) random environmental effects. The expected environmental value of individuals which rank in the upper 0.01% of the population is equal to c^2 (60).

The coefficient of environmental determination may also be used to predict the change that may occur in a population when offspring develop in a "selected" environment, i.e., in an environment in which measured non-genetic effects are completely controlled. For example, let us assume that a random sample of children were reared in the same measured environment as individuals in the upper 0.01% of the population of the previous generation. Since these children were chosen at random, the expected phenotypic value would equal the expected environmental value of individuals in the upper 0.01% of the population. Therefore, the mean IQ score of these individuals should average (c^2) (60) above the mean of the previous generation. Of course, unlike genetic selection, this new environment would have to be maintained in order to sustain this change. Although no estimate of c^2 is available, let us assume for illustrative purposes that the heritability (h^2) of performance on this test is 0.5 and that c^2 is 0.25 (the remaining 25% of the variance being due to both non-additive gene effects and to unknown environmental causes). Therefore, children reared in the measured environment of individuals in the upper 0.01% of the population would be expected to score (c^2) (60) = (0.25) (60) = 15 IQ points above the over-all mean of the previous generation.

The effects of environmental selection on individuals which are not randomly selected from a population may also be estimated. In such prediction equations, the genotype, as well as the environment, must be considered. From the model, it may be seen that the expected phenotypic value ($\hat{P}$) is merely equal to the sum of the expected additive genetic value ($\hat{A}$) and the expected environmental value ($\hat{C}$), since $\hat{E} = 0$. If the population were subdivided into different racial groups, the estimate of A would be based upon the deviation of the phenotypic value of the individual from the mean of its group (P_W) and the deviation of the group mean from the population mean (P_f), each weighted according to its respective heritability. An analogous c^2_W and c^2_f could also be formulated. However, for the sake of simplicity, it shall be assumed that the population is not subdivided into such groups.

Let us, for example, consider the effect of environmental selection on the performance of children from "culturally disadvantaged" homes, where the average IQ test scores of the parents is 20 points below the mean. If the children were reared under the same measured environmental conditions as the parents, they would be expected to average $b_{AP}(P) + b_{CP}(P) = (h^2 + c^2)\ (P) = (.50 + .25)\ (-20) = -15$ or 15 IQ points below the mean of the population. If, however, these children were allowed to develop under average environmental conditions, the expected environmental value would be zero; hence, they would be expected to score only $(h^2)\ (-20) = (.5)\ (-20) = -10$ or 10 IQ points below the mean. But what would be the expected performance of these children if they were reared under an enriched environment, e.g., the measured environment of individuals which scored in the upper 0.01% of the population? These children should average $(h^2)\ (-20) + (c^2)\ (60) = (.50)\ (-20) + (.25)\ (60) = 5$ IQ points above the mean of the population.

Discussion

A simple extension of the usual quantitative genetic model permits the formulation of a new population parameter, the coefficient of environmental determination. This parameter, symbolized c^2, has both descriptive and predictive roles: It indicates the relative importance of measured environmental effects as causes of individual differences in a population and also may be used to predict the change that will occur when a population develops in a selected environment. Such predictions may be of doubtful value due to the impossible requisite of complete environmental control. However, such estimates may suggest the feasibility of changing the mean phenotypic value of a segment of the population by the control of existing environmental variation. If c^2 were large, much change could result from control of existing environmental variation. If c^2 were small, little change would result from such control.

However, it is important to note that a low value for c^2 would not necessarily imply that deficiencies could not be compensated by environmental factors. A low c^2 would merely indicate that measured environmental factors were not important causes of individual differences in the population. Thus, although control of measured environmental effects would not result in a substantial change in the mean phenotypic value when c^2 is low, special environmental regimes (e.g., therapy, diets, special education, etc.) might still be effective. It is also important to recall that c^2 is a population parameter which, like h^2, may vary from character to character in the same population, from population to population for the same character, and from time to time for the same character in the same population.

No valid estimate of c^2 is currently available. In fact, even available estimates of h^2 for behavioral characters in human populations are of doubtful validity. Human relatives share a common environment. Therefore, the resemblance between relatives in the human population will almost certainly result in overestimates of h^2 unless the environmental contribution to the similarity is removed. However, it would seem that valid estimates of both h^2 and c^2 are obtainable for human behavioral characters. Such estimates could be obtained from large-scale family studies where behavioral scores on a large number of parents and their children are assessed and where the environment in which the children developed is indexed as accurately as possible.

Summary

Although quantitative genetic theory was primarily developed for application to animal and plant breeding, its concepts and methods are applicable to important social issues. The heritable nature of group differences may be expressed as a function of the within-group heritability. Application to IQ data demonstrates that a high within-group heritability does not imply that the observed difference between the means of Afro-Americans and Caucasians is also highly heritable.

The quantitative genetic model may also be extended to include measured environmental effects. This extended model facilitates the formulation of a new population parameter, the coefficient of environmental determination, which is defined as the proportion of the total variance for some character in a population which is due to measured environmental effects. This variance ratio, analogous to heritability, has both descriptive and predictive properties. It may be utilized as an index of the value of the environment in which an individual developed and to predict the effects of controlling environmental variation in a population.

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Table 1. Values of h_f^2 as a function of h_w^2 and r, assuming t = 0.20.

h_w^2	r											
	.001	.002	.004	.008	.01	.02	.04	.06	.08	.10	.20	.30
.4	.002	.003	.006	.013	.016	.03	.07	.10	.14	.18	.40	.69
.6	.002	.005	.010	.019	.024	.05	.10	.15	.21	.27	.60	---
.8	.003	.006	.013	.026	.032	.07	.13	.20	.28	.36	.80	---

HUMAN BEHAVIORAL ADAPTATIONS - SPECULATIONS ON THEIR GENESIS

by

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HUMAN BEHAVIORAL ADAPTATIONS - SPECULATIONS ON THEIR GENESIS

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It is presumptuous to talk about the evolution of any primate characteristics let alone the evolution of human behaviors among *echt* scientists. But like the rodent and the cobra, we may temporarily take pleasure from the excitement and fascination of the confrontation and take our chances with being consumed. As has often been noted, behavior leaves no fossils; it was paleontology that did so much to legitimize the scientific (as opposed to the philosophical) credence in Darwinian theory. Unfortunately, we behavioral evolutionists have no tool more powerful than analogous reasoning and little unassailable evidence. A few years ago, Bullock (1963; see Moore, 1970) introduced his paper on the physiological basis of behavior to the XVI International Congress of Zoology with the following paragraph:

> The gulf between our present level of physiological understanding and the explanation of behavior as we see it in higher forms is wider than the gulf between atomic physics and astronomy and is indeed the widest gap between disciplines in science. But real understanding of behavior is the great challenge of the future, not only for biology but for all sciences. It cannot wait for full development of the basic sciences on which it eventually rests, but must proceed, as it is proceeding, simultaneously on all levels (p. 451).

Although we can use such words as an amulet, we would like to present one further caveat to remind us of our vast ignorance of how natural selection operates to produce evolution (i.e., in practice not in principle). C.C. Li (1970), in discussing human genetic adaptation, said,

> "Most of the selection models so far studied by geneticists are limited to one pair of genes. In fact, a general solution for selection with respect to two pair of genes has not yet been obtained and is still under active investigation, despite the liberal use of high-speed computers (p. 561)."

Since virtually all behavioral traits of interest in man will be under both polygenic genetic and environmental control, our paper must of necessity consist largely of speculations about the evolution of human behavior. Hopefully the elucidation of a few principles of evolution found useful for understanding non-behavioral traits will justify the inclusion of this morning's deliberations in a program oriented around basic research in education.

General Considerations: Evolutionary Outcomes and Kinds of Selection

Adaptedness is a product of evolutionary development which is maintained and can be improved by natural selection. Natural selection is the force underlying evolution; the essence of natural selection is the differential reproduction of genotypes best adapted to the demands of the environment. You may either accept the teleology involved here or spend a lifetime grappling with it (cf. Dobzhansky, 1970). Selection occurs in many different forms with different consequences. First there is stabilizing or normalizing selection which works to maintain the status quo of a population's gene pool; it is a conservative force, not to be ridiculed, rather like investing only in government bonds. Then there is balancing selection which adds another technique for maintaining genetic variability; it permits genes to stay in the population even though they have bad effects in double doses because in single doses they appear to confer some kind of advantage in some environments. This kind of selection acts like a kind of premium paid for disaster insurance; it hurts to pay it, but it pays off if the disaster ever comes. Of most importance to a discussion on the evolution of human behavior are directional selection and diversifying selection. The former causes the composition of the gene pool to change or shift in some particular direction so as better to accommodate to changes which have occurred in the environment (it will also preserve fresh mutations which work better than the old ones even if the environment didn't change). The latter, diversifying selection, seems to us to just be "multidirectional" selection, a kind that simultaneously favors two or more phenotypes in an environment with multiple niches. Such a process leads to sexual dimorphism, the formation of sub-species, incipient species or new species.

It is immensely important when talking about the possible roles for selection pressures in molding the shape of a gene pool to remember that natural selection operates on the total organism (the phenotype) with indirect effects on the gene pool of the following generation. The Darwinian fitness of an individual (i.e., the number of offspring he has) is the net result of the sum of his assets and liabilities in his particular environment. The corollary of this proposition is that man is simultaneously being subjected to selection pressures from many selective forces. A widespread misapprehension about how natural selection works may stem from the wider familiarity of the public with artificial selection for one economically useful character at a time in domesticated animals, forgetting that the breeder can easily eliminate the ones which don't suit him.

A Brief Overview of Primate Phylogeny

Thinking in evolutionary terms requires some perspective of the time periods involved and the relative position of the phylogenetic branches.

With the development of methods for determining the sequence of amino acids in proteins, a new tool was added to the study of evolution. Because a mutation at a structural locus may result in the substitution of one amino acid for another in the completed protein, tracing the variation in a protein through a group of organisms and counting the number of amino acid substitutions gives an estimate of the relative distance in time separating the species (an evolutionary protein clock). For example, human hemoglobin and chimpanzee hemoglobin are the same. Gorilla and human hemoglobin differ in two amino acids, men and monkeys differ in 12 amino acids and men and horses in 43 amino acids (Wilson and Sarich, 1969). Figure 1 indicates the evolutionary paths that seem most likely for man and some of his closer primate relatives as well as rough estimates of divergence times.

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Insert Figure 1 Here
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Evolution of Brain Size and Tool Use

Thiessen said (1971) that, "There is little investigative hope of constructing a phylogenetic tree to express the evolutionary trends of behavior. Evolution (of behavior) has not been progressive or linear and has not occurred at uniform rates....There is more hope, it seems to me, in dealing directly with species-specializations and treating them as evolutionary reflections of ecological demands." We agree. One line of evidence that must be pursued is the evolution of brain.

Jerison (1963) has estimated the number of adaptive neurons in mammals of different sizes using information on brain and body weight; the method allows the eight major primate taxa to be distinguished from each other but not between closely related species or genera. Adaptive neurons are those left over after basic "housekeeping", for example, moving muscles and maintaining visceral function. The results of the method are given in Table 1. It is obvious that the numbers of neurons have increased tremendously in hominid evolution. Keeping in mind the numerous speculations and approximations that have entered into the Jerison technique, it still manages to show a difference in the predicted direction between erectus and the anthropoid apes despite similarity in brain size. It also demonstrates the predicted similarity between chimpanzee and gorilla despite a difference in body weight.

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Insert Table 1 Here
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The increase in "discretionary" neurons (roughly) parallels increasing ability to make and use tools, even though gigantic strides and sophistication appeared after the level of 8.5 billion adaptive neurons was reached near the end of the Middle Pleistocene some 100,000 to 200,000 years B.C.*

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*We ask forgiveness if these dates and others have again changed since our data sources were published.

The archeological record suggests that there was little improvement in the pebble tools used by Austalopithecine at the beginning of the Lower Pleistocene some two to five million years B.C. until the flake tools of Homo erectus in the Middle Pleistocene roughly a half million years B.C. Buettner-Janusch (1966) interpreted this to mean that the rather abrupt change in the "tool kit of man" (if it was abrupt) was not associated with a stepwise increase in adaptive neurons, perhaps because a sufficient threshold number had been reached permitting the adaptive capacity necessary for diversity and elaboration of tools. The degree of correlation between evolution of brain and tool manufacture is vague; the evolution of culture may have been as important or more so as a selection pressure favoring brain size.

> "Once the neurological capacity to symbolize and to make culture evolved, the differentiation and rapid development of culture itself very likely put severe demands upon the brain....This probably required elaboration of the cerebral cortex, a larger set of association neurons and interconnections between them (Buettner-Janusch, 1966, p. 352)."

It is easy to imagine that even with tools at his disposal, early man required massive changes in social organization--the formation of a hunting group--which in turn demanded efficient communication, cooperation among males and role specialization, planning ability, and longer term memory storage. To quote Buettner-Janusch again,

> "The lineage of primates in which all these capacities were presumably developing would be under strong selection pressure to continue to develop and refine such traits, in an environment rapidly changing from forest to open bush and plains (p. 360)."

Anthropologists disagree among themselves as to the relative importance of bipedalism, tool use, and social organization as selection pressures favoring increasing brain size (Washburn & Avis, 1958). We leave the intriguing data in Table 1 on the elephant and porpoise to the discretion of our anthropoligist-geneticist-anatomist discussant, Professor Pollitzer.

Further discussion and references about the evolution of neocortex may be found in Diamond and Hall (1969) along with a very clear example of the results of convergent evolution on the visual system of squirrels and tree shrews (the "lowest" living primate), unrelated species occupying similar ecological niches. These animals have independently developed visual systems that are virtually identical. Similar environments produce similar organisms. This provides a concrete example of the Markov chain principle as discussed by Li (1970). Once similar end points have been attained by two populations, for many important purposes their past evolutionary history does not matter.

Ernst Mayr (1963) has applied the term mosaic evolution to the process whereby each organ and each system of organs has its own rate and pattern of evolution. Mosaic evolution characterizes the form of genetic response which follows a move into new adaptive zones; it supports the view that man became what he is today very, very gradually. Phylogeny in relationship to the evolution of behavior is discussed cogently by Hodos and Campbell (1969).

Within Species Behavioral Variability

All men belong to one species, but races of men or other Mendelian populations can be thought of in some respects as incipient species. Homo sapiens has failed to speciate for two main reasons.

> ...man's great ecological diversity. Man has, so to speak specialized in despecialization. Man occupies more different ecological niches than any known animal. If the single species man occupies successfully all the niches that are open for Homo-like creatures, it is obvious that he cannot speciate. The second reason is that isolating mechanisms in hominids apparently develop only slowly....The probability of man's breaking up into several species has become smaller and smaller with the steady improvement of communication and means of transport. The internal cohesion of the genetic system of man is being strengthened constantly. Mayr, 1963, pp. 643-644.

From an evolutionary viewpoint we are interested both in genetically conditioned homogeneity (species-specific characteristics) as well as genetically conditioned heterogeneity (non-species-specific characteristics). It can be hypothesized that the former evolved through parallel and convergent evolution while the latter evolved through divergent evolution.

Thiessen (1971), speaking as a comparative animal behavioral geneticist has made a cogent case to the effect that traits related to fitness show a restriction of genetic variability (and low heritabilities). He suggested that polymorphisms observed in a species' gene pool may be functionally equivalent. From this he made the provocative suggestion that traits with high heritabilities may be "genetic junk". It has been observed by animal breeders (Lush, 1945) that artificial selection for a trait uses up its additive genetic variance and leads to low heritabilities. These ideas may serve as points of discussion by this group. Although we agree with Thiessen in respect to other animals, in defense of our serious interest in within Homo sapiens variability, we must point out that we have no way of knowing in advance whether trait differences between populations reflect directional or diversifying selection, a transient polymorphic state of affairs, or non-genetic adaptability. We think that a better understanding of human behavior may result from such concerns.

Our species-specific curiosity and self-awareness make us want to know about the meaning and significance of our non-species-specific and fascinating diversity. Such a stance also permits us to discern the directions in which man is continuing to evolve. One of the goals of our paper is to stimulate discussion about the circumstances that could have led both to similarities as well as differences in the genetic bases for human behavioral traits within and between Mendelian populations.

Adaptability and Genotype-Environment Interaction

Given the well-worked out example of the relationship between the gene for sickle cell hemoglobin and heterozygote advantage in a malarial environment, it is too easy to jump to the conclusion that other genetic polymorphisms are also maintained by some kind of selective advantage. Other examples, however, are exceedingly scarce. The genetic diversity of man has been amply demonstrated but is hardly understood. We have good evidence based on enzymes and red cell antigens in humans that about 30% of all our genetic loci may be polymorphic; except for the one example of Hb^S, and possibly a few others, we do not know what maintains the remaining polymorphisms and do not understand the physiological function of the alleles involved. Do the kinds of phenotypic differences we see among races or Mendelian populations also imply selection pressures in their ancient histories with consequent changes in their genotypes? It turns out that it is very difficult to distinguish between changes due to behavioral and physiological adaptibility and those due to changes in adaptedness via natural selection leading to gene pool changes (cf. Ayala, 1970, Dobzhansky, 1968). A concise treatment of the difficulties may be found in Lorenz's (1965) essay Evolution and Modification of Behavior.

As an example of the problems, the increased height in Japanese children born to Japanese parents in the USA compared to those born in Japan is well documented (Greulich, 1957). It is a good example of (assuming no selective migration) a phenotypic change not associated with a genotypic one; it is an example of the reaction range concept (Gottesman 1963, 1968) with the improved pre-and post-natal environment in the USA Japanese promoting a changed phenotype. Height is an excellent trait for model building in that it is under both genetic and environmental control. The reaction range concept builds on the classical work of Clausen, Keck, and Hiesey (1948) who planted different races of plants together (genetic heterogeneity + environmental homogeneity) and transplants of the same plant in different environments (genetic homogeneity + environmental heterogeneity). Two important axioms of the reaction range concept are the following: (1) Different genotypes may have the same phenotype (observed characteristic) and (2) Different phenotypes may have the same genotype (i.e., for the trait under consideration). Figure 2 illustrates the concept with respect to human height (Greulich, 1957; Meredith, 1969; Mørch, 1941) although it can be generalized to such traits as IQ score (cf., Gottesman, 1963). The units for both X and Y axes are only ordinal and not to scale.

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Insert Figure 2 Here
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Each curve in the figure can be construed as representing the phenotypic response of samples of individuals homogeneous for four different levels of genetic potential for height who have been reared in various trait-relevant environments (or niches) crudely characterized as restricted, natural habitat, and enriched. Curve Type A could represent a deviant genotype, for example, the one associated with the dominant gene for chondrodystrophic dwarfism which has an incidence at birth of 1 in 10,000. The different environments to which such dwarfs have so far been exposed do not have much effect on their height; the mean height for 15 year old cases (sexes combined) is only 120 cm. Curve Type B could represent samples of thirteen year old Japanese girls: in contemporary Japan they average 146.1 cm; (="natural" habitat) thirteen year old girls measured in post-war Japan (1950) only averaged 139.9 cm. (= restricted environment nutritionally); thirteen year old Japanese girls born in the USA to Japanese parents averaged 150.5 cm. (= enriched environment). The Reaction Range (RR B) for the genotype represented by thirteen year old Japanese girls under the range of environments sampled would be the largest value minus the lowest or 10.6 cm. Curve Type C could represent the response of the genotypes of fifteen year old Japanese boys measured at the same times as the girls in B; we are dealing here with sexual dimorphism and a different genotype (pace women's lib) for height. Post-war boys averaged 151.1 cm; contemporary boys in Japan, 158.2 cm.; and, contemporary Japanese boys born in the USA, 164.5 for a reaction range of 13.4 cm., all attributable to environmental variations. Curve Type D could represent 15 year old US white boys who average 168.7 cm. (13 year old white girls average 155.4 cm.). Examples of the same phenotype with different genotypes are provided by some data on children of Japanese US white matings (fathers always white); the 15 year old boys averaged 164.7 cm. while the 13 year old girls averaged 151.5. It appears that the hybrids matched the US born Japanese and were about halfway between contemporary Japanese and white children (under natural habitat conditions). Other genotypes could have been added to Figure 2 for such diverse groups as the Mbuti pygmies and Nuer of Sudan with adult mean heights of 144 cm. and 184 cm., respectively. The thrust of the reaction range concept is that both heredity and environment are important in determining trait variation but in different ways, combinations, and degrees, some of which are amenable to dissection for some traits.

A particularly instructive example of adaptibility in the face of selection pressure without, apparently, a genetic change is given by Harrison's (1967) work in Northern Ethiopia. Two populations of Amharic Ethiopians were shown to be essentially similar genetically by similar blood groups and because there were high migration rates between the two populations; who are only separated by a short geographical distance. However the homeland elevations involved are 5,000 and

10,000 feet. Such a difference in altitude would be expected to exert differential selection pressures on the two groups. At 10,000 feet there was lowered partial pressure of oxygen and colder temperatures; at 5,000 feet malaria, dysentery, and measles were much more common. We will only report some of the morphological differences between the highlanders and lowlanders. The former were heavier and had greater chest circumference and antero-posterior and transverse chest widths. Harrison found that the parameters were not only modifiable during growth but also in adulthood; adult migrants to the highlands showed a morphology similar to the indigenous highlanders. The enlarged chests were due to hypertrophy of the intercostal muscles. Migrants to the lowlands lost some of their adaptibility and were intermediate in morphology. The important lesson in these data according to the investigator was that they showed that these differing ecological niches did not require evolutionary change. Adaptability was all that was needed.

As this is being written two more men and working on the surface of the moon, a very inhospitable ecological niche. We did not have to breed a new race or genotype for that niche; the adaptive potential of the *Homo* genotype, selected for plasticity and greatly extended and multiplied by technology, permits such phenotypic diversity. These kinds of examples can be seen many times over in Baker and Weiner's (1966) *The Biology of Adaptability* and lead us to counsel caution before automatically ascribing phenotypic differences in biologically based traits to genetic differences.

We now turn to the opposite sort of error. Some behavioral differences between Mendelian populations of Homo sapiens may be associated with genetic differences.

One of the many working hypotheses in a discussion of the evolution of human behavior is that cultural transmission is man's principal instrument of adaptation. At our present state of knowledge, this is only opinion. Although culture is transmitted non-genetically via learning, it has a genetic foundation that characterizes our species and which evolved genetically. With a few pathological exceptions, it can be argued but not proved that selection pressures were uniform across whatever races existed in the Middle Pleistocene for the general properties of educability, and the capacity to learn from positive and negative reinforcement (cf. Caspari, 1958; Dobzhansky, 1962). It is not empty diplomacy to talk simultaneously about genetic and cultural evolution of behavioral traits. To quote Dobzhansky (1969),

> "Culture proved to be an adaptive contrivance more potent than any other which appeared in the whole evolutionary history of life. This does not make genetic development superfluous. However, genetic adaptation is shifted, so to speak, at two removes from the environments which the human species has to face. Genetic evolution enhances the efficiency and the openendedness of the non-genetic, i.e., cultural evolution (p. 290)."

As an illustration of this interaction, Dobzhansky sketched a scenario about the invention of the use of fire by Homo erectus in eastern Asia during the Middle Pleistocene.

> Here was an adaptive achievement of a highest order, symbolized in the myth of Prometheus. Did this race possess a special Promethean gene, which other races had to acquire before they too could use fire? This is unlikely. The inventors and their disciples had, however, a common genetic system which enabled them to

> learn and to transmit what they had learnt. It makes little difference to the argument if we suppose that the race Homo erectus pekinensis had a better, or only an equally good, genetic equipment for learning and transmission of learned information as did other races of the same species. (p. 290)

But don't let the story end there, for the case can also be made and has, that natural selection can "shape" behavior just as it has shaped say protective coloration in the famous example of industrial melanism in moths. Tinbergen (1963, see Moore, 1970) has issued a number of warnings which we can paraphrase as follows:

1. Do not assume a behavior is without adaptive value unless you have ruled it out by observations, preferably in a natural setting.
2. Do not be too quick in blaming differences between groups on genetic drift.
3. Do not be too quick to attribute the presence of a character merely to pleiotropism.

The plain fact is we usually cannot choose between the alternatives presented.

The Evolution of Milk Drinking

Darwin in his The Descent of Man (1871) suggested a strategy for making choices and anticipated modern developments in human genetics when he commented on the relationship between hair and skin color and immunity to tropical diseases. He had observed that white settlers in Africa died of malaria and yellow fever while natives did not and that Sudanese recruited to fight in Mexico also escaped them. "That the immunity of the Negro is in any degree correlated with the colour of his skin is a mere conjecture," he said but then proceeded to design a research project which was never completed. In the spring of 1862 he obtained permission from the army to elicit information from the surgeons stationed with troops in tropical areas about the hair color of Englishmen affected with dysentery, malaria, and yellow fever. He concluded his request with this prophetic comment,

> "Theoretically the result would be of high interest, as indicating one means by which a race of men inhabiting from a remote period an unhealthy tropical climate, might have become dark-coloured by the better preservation of dark-haired or dark-complexioned individuals during a long succession of generations."

Another trait in which human populations differ is the concentration of the enzyme lactase. It is the only common trait known at both the biochemical and behavioral levels that contributes to "normal" variability in both. Although even here there is much that remains to be learned, lactase provides a reasonable model of divergent evolution. We owe much of our understanding to reviews of the subject by McCracken (1971) and Simoons (1970).

Lactase is an enzyme active in the villi of the small bowel and lactose is the main sugar in milk. Lactase splits the disaccaride lactose into the monosaccarides glucose and galactose. Monosaccarides can be absorbed into the portal circulation but disaccarides cannot. In the absence of lactase, ingested lactose simply passes through the gut without providing nutrition. If too much is ingested, cramps and diarrhea result.

While the clinical syndrome has been recognized for some time, its genetic basis has only recently become apparent. That the enzyme deficiency is a genetic and not an acquired trait produced by lack of dietary milk now seems established. The evidence is provided by a study of Thai children living in an orphanage where milk was fed from birth. By age two all were lactose intolerant (Simoons 1970). Family studies which are few in number but consistent, (Ferguson and Maxwell, 1967; Fine, et al, 1968; Flatz and Saengudom, 1969; Welsh, et al, 1968) suggest a two or possibly three allele locus. One allele is sufficient to maintain lactase production throughout life. Homozygotes for a second allele cease producing lactase after infancy or early childhood. Thus tolerance for lactose is a dominant condition. It is possible that a third allele may be associated with a rare recessive, usually fatal trait, infantile milk intolerance. Afflicted babies never produce lactase. On the basis of present evidence the most likely situation is as indicated in Table 2.

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Insert Table 2 Here

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The evolutionary significance of lactase is suggested by the very striking differences in the distribution of phenotypes. In general, European populations digest and absorb lactose and thus can utilize milk as food. Asian, Amerindian, and African populations on the other hand are generally lactose intolerant. The proportion of tolerants is 90-100% in northern Europe and zero-10% in most of the rest of the world. It is quite important for educators and dietians to apprehend that just because milk is good for babies it may not be good and in fact will be harmful for some children. The milk-break and school lunch programs will make many of our black, brown, red, and yellow children ill. Notorious examples can be cited of disadvantaged peoples in underdeveloped countries using powdered milk (it has even more lactose than fresh milk) to whitewash their houses. Contrary to the advertising slogan, not everyone needs milk!

There are informative exceptions to the general distribution of lactose intolerance described earlier. African and Asian herders and cattle raisers are lactose tolerant. Such groups can be found living in areas adjacent to those occupied by a lactose intolerant population. Also, the Caucasian population on the southern rim of Europe has a high proportion of lactose intolerant persons. In general, groups utilizing milk for food tolerate lactose while groups who historically have not utilized milk for food do not tolerate lactose. A few examples of population prevalences are given in Table 3.

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Insert Table 3 Here

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Selection for lactose intolerance must have begun 10-12 thousand years ago when human populations began domesticating milk-producing animals. Because the adult form of intolerance is not fatal and would only be disadvantagous when food supplies were very marginal (sour milk and some milk products such as yogurt or cheese are digested by intolerant persons) selection pressures must have been gentle. We may also note that selection favoring tolerance must have increased in populations where significant numbers had already become tolerant: the possession of a favorable trait increasing fitness lends to displacement of the other gene. Once some members of the population utilize milk as a food, the remaining members were at an increased disadvantage.

As in other examples of interaction between environment and genes the more one understands about this specific phenomena, the more difficult it becomes to separate genes from environment. In the case of lactase it appears that a cultural-technological advance, domestication of animals, was inexorably intermeshed with a change in gene frequency. At the same time, the cultural-technological advance must have accelerated the genetic change. The range of cultures and individual behaviors entailed by this genetic-environmental change is obviously extremely broad with ramifications into almost all aspects of life.

It appears that primitive man, like all mammals, must have been lactose intolerant after infancy. It is toleration for lactose that must have evolved. We may ask then what magnitude of selective advantage would have been required to change the frequency of a favorable dominant mutation to currently observed levels. Accepting the current prevalence of lactase deficiency in contemporary intolerant populations to be 90% as opposed to a 10% in northwestern Europe, the corresponding frequencies of the gene for adult lactase production would be .05 in intolerant populations and about .60 in tolerant populations. With the help of a table provided by Lush (1945) we were able to work out an approximate selection intensity against homozygotes (2-2) required to produce a change in gene frequency from .05 to .60 in the 400 generations since domestication of sheep and goats. The selection intensity is approximately .01. The literal meaning of this number is that if lactose tolerant persons had an average of 1% more children per generation than lactose intolerant persons, the observed change in phenotype frequency could occur in the time available. The value .01 is a common one in the literature and therefore not an unreasonable one. Table 4, reproduced from Lush, provides useful insights into the problems involved.

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Insert Table 4 Here
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A few other traits deserve mention. The studies of Post (e.g. 1964) have suggested that color blindness is more common in populations that have been longest removed from the hunter-gatherer stage of civilization. Similar relationships have been found in visual and hearing acuity and in the incidence of nasal septum deviation.

While we think there is much to be learned from the study of single locus and relatively simple traits, behavioral traits are mostly polygenic and selection acts on phenotypes. We have, we conclude, no wholly satisfactory models of selection for any polygenic traits in man, let alone behavioral ones. The most conspicuous candidate is skin color which appears to be due to 4-5 gene pairs acting in accordance with an additive polygenic model (Stern 1970). We have theories seeking to account for the differences in skin color we observe in different populations but the critical physiological evidence to back the theories is lacking. Dark skin probably confers some protection against skin cancer and it may prevent overproduction of vitamin D. Dark skinned eskimos have a unique diet with ample vitamin D. They therefore did not need to evolve white skin. Although it seems evident that the differences among races are due to diversifying selection pressures, we cannot specify the pressures and hence the model is incomplete.

What Next?

How can our ignorance be remedied? Being aware of the evolutionary process leads us to ask questions about the evolution of human behavior. We have few answers and perhaps only now are prepared to look seriously. But we are painfully aware that other disciplines sharing the behavioral science niche likewise have no answers. How much further might we be in our understanding of human learning had all the man-years devoted to the laboratory white rat been spent with tree shrews? What might be learned if we admitted that races of men are Mendelian populations whose racial hybrids form natural experiments providing evidence (in certain circumstances) of genetic differences in behavior between the parental populations?

What would happen if social scientists recognized aggression as a behavior with a long evolutionary history in our (and nearly all other) species; the ethologist would quickly point out that altruism has an equally long history and that perhaps man is subject to contradictory motivations. Homo sapiens in all our glory has evolved as a conglomerate of compromises; it is not a form of condescension to deal with members of our species via compromises. It is rather a cultural adaptation required by our genetic adaptedness.

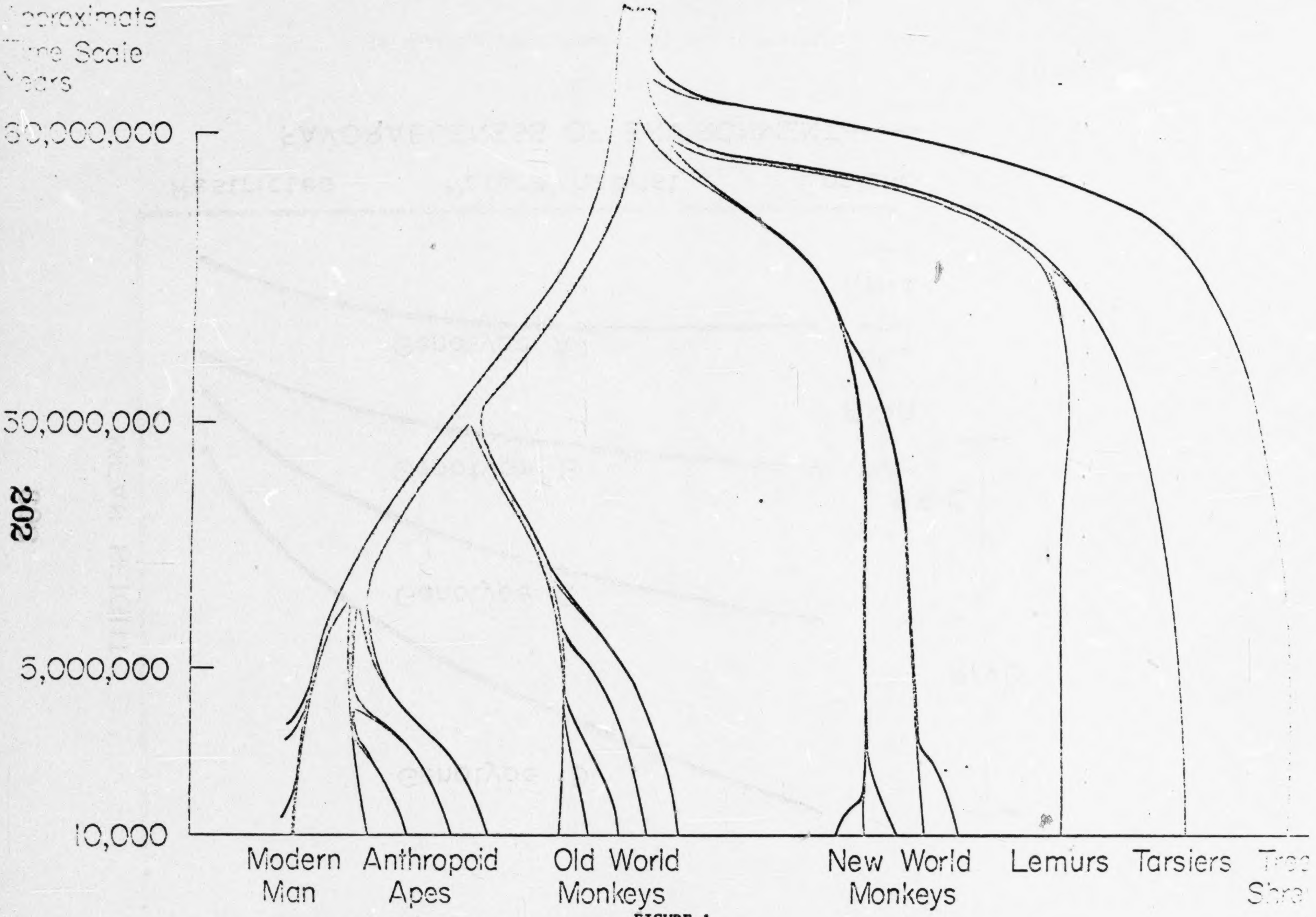
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FIGURE 1
Approximate Temporal and Biological Relationships Between Major Primate Groups

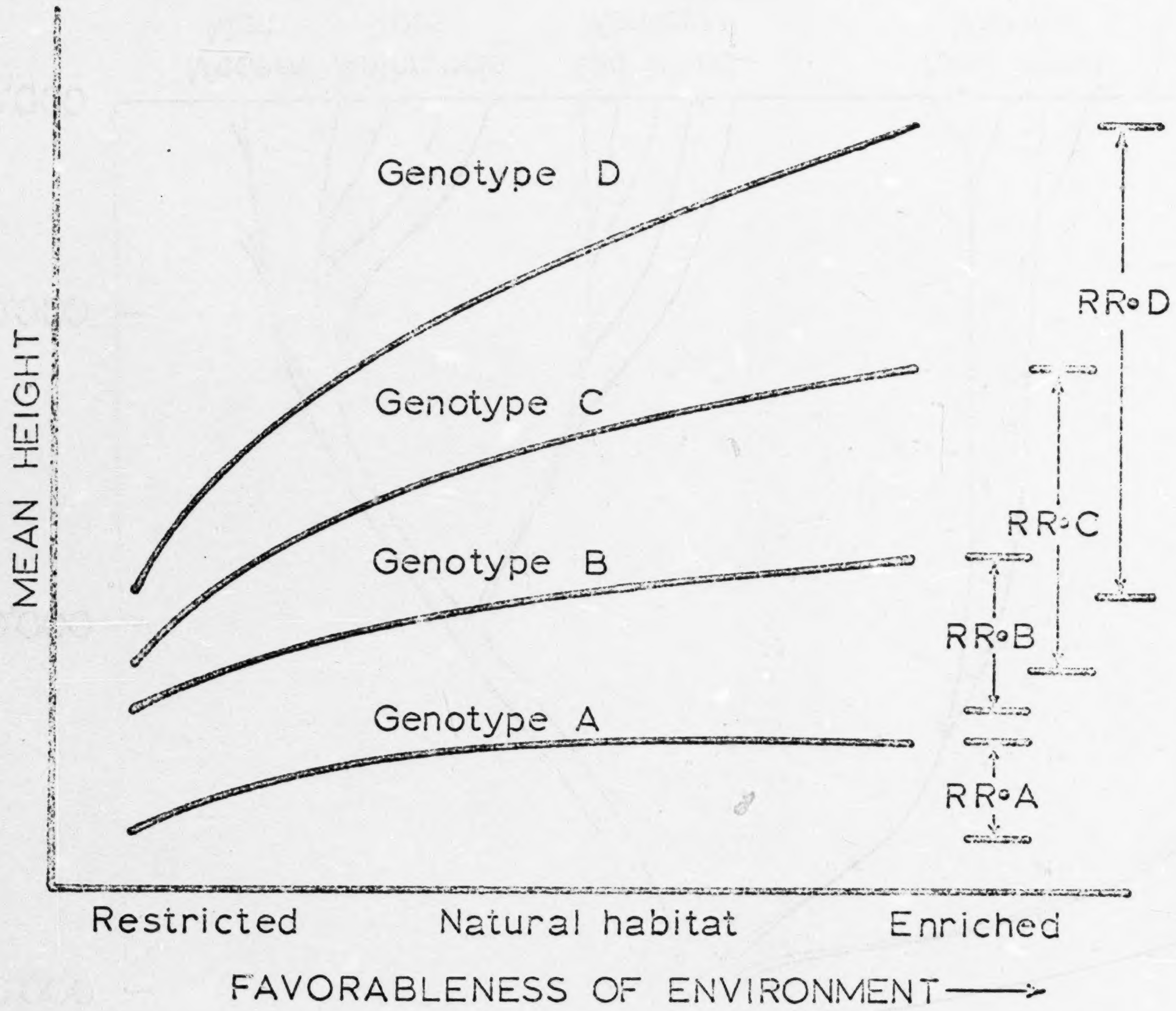

FIGURE II

The Reaction Range Concept Applied to Height

TABLE 1

Estimates of Adaptive Cortical Neurons in Mammals of Different Brain and Body Sizes

Adaptive neurons are those cortical neurons associated with the adaptive capacity of the brain. (After Jerson, 1963.)

Animal	Brain Weight	Body Weight	Number of Adaptive Neurons
Macaca (Rhesus)	100 g	10,000 g	1.2 billion
Papio (Baboon)	200	20,000	2.1
Pan troglodytes (Chimpanzee)	400	45,000	3.4
Pan gorilla	600	250,000	3.6
Australopithecus	500	20,000	4.4
Homo erectus	900	50,000	6.4
Homo sapiens	1300	60,000	8.5
Elephant	6000	7,000,000	18.0
Porpoise	1750	150,000	10.0

TABLE 2

Possible Genetics of Lactase System

Lactase Genotypes	Phenotype Effect
1-1	Lactase Present Through Life
1-2	Lactase Present Through Life
1-3	Lactase Present Through Life
2-2	Lactase Deficient After Infancy
2-3	Lactase Deficient After Infancy
3-3	Infantile Milk Intolerance (Rare, usually Fatal)

TABLE 3

Prevalence Lactose of Handling Phenotypes*

Population	N	Percentage Tolerant	Percentage Intolerant
Australia (Aborigines)	44	15	85
Australia (Europeans)	160	96	4
Amer. Indian	24	0	100
Amer. Caucasian	245	88	12
Amer. Negro (Baltimore)	20	5	95
Chinese	71	7	93
Bantu	59	11	89
Thieu	179	2	98
Finnish	134	82	18

*Data mostly from McCracken and Simoons

TABLE 4

Approximate Time Required for Selection to Increase the Frequency (*q*) of a Favored Gene by Various Amounts (from Lush, 1945)

q to be Changed from q_1 to q_2		Time, Expressed in 1/*s* Generations			Correction Factor *x*
q_1	q_2	Selection for a Complete Dominant (*h* = 0)	Selection When There Is No Dominance (*h* = .5)	Selection for A Complete Recessive (*h* = 1.0)	
.01	.05	1.69	3.30	81.65	1.61
.05	.10	.81	1.49	10.75	.69
.10	.20	.95	1.62	5.81	.69
.20	.30	.72	1.08	2.21	.41
.30	.40	.68	.88	1.28	.29
.40	.50	.74	.81	.91	.22
.50	.60	.91	.81	.74	.18
.60	.70	1.28	.88	.68	.15
.70	.80	2.21	1.08	.72	.13
.80	.90	5.81	1.62	.95	.12
.90	.95	10.75	1.49	.81	.05
.95	.98	30.95	1.89	.98	.03
.98	.99	50.70	1.41	.71	.01
.99	.995	100.70	1.40	.70	.00
From answer in generations subtract:		*x*	2*x*	*x* + $1/q_1 - 1/q_2$	

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GENETIC DETERMINATION OF BEHAVIOR (ANIMAL)

by

Gerald E. McClearn

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THE COMPARATIVE METHOD

It is not often the case that research conducted on some non-human animal species is motivated solely by interest in that species *per se*. To some extent, explicitly or implicitly, the results are expected to have some degree of phyletic generality. In general, evolutionary theory provides the basis for expecting some generality. If each species were separately created, there would be no particular reason for expecting common principles from one to another.

No biological discipline has had greater success in the comparative approach than has genetics, where the spectacular advances in understanding of the nature of inheritance of the whole spectrum of living forms have come from (among others) peas, Drosophila, Neurospora and bacteriophage.

For our present topic we need to inquire also about the comparative method in behavioral research. In parts of Psychology the results of animal research have been readily accepted but in other parts of the field, and in some other social and behavioral science disciplines, the relevance of animal data to man has been challenged on the ground that, once man developed culture, he became something apart from the rest of the biological world, and exempt from the rules applicable to that world. In the simple-minded expression of the nature-nurture controversy, many felt that there were two opposing teams and that one had to choose sides. Because culture has an undeniable influence, many social scientists therefore came to reject "nature's" influence entirely. Nowadays, this dichotomous view is no longer supportable, and the interaction and mutual action of genotype and environment, both in generating variability within populations and in the evolutionary process, must provide the conceptual framework. New perspectives in Physical Anthropology have also clarified the gradual nature of the development of culture and of the evolution of the human brain to cope with a given level of culture and to generate more. There has been, in effect, a mutual boot-strapping operation. First steps toward culture provided a new environment in which some individuals were more fit, in the Darwinian sense, than others; their offspring were better adapted to culture and capable of further innovations; and so on. The argument can be made that, far from removing mankind from the process of evolution, culture has provided the most salient natural selection pressure to which man has been subject in his recent evolutionary past.

However, a simple ladder conception of evolution, with species arranged in a unidimensional array, won't suffice in evaluating the comparative approach. The branching and sub-branching of the phylogenetic tree leads us to expect that some characters will be quite general and that others will be quite restricted. Lacking advance notice, the test will be a pragmatic one. It would seem, therefore, that data from a non-human source should be viewed as suggestive with respect to man; one should be neither too eager to generalize to man nor to deny potential relevance.

Another related objection sometimes raised with respect to the comparative method in behavior is that the animal model may be an incomplete representation of the human situation. For example, the possibility of relating animal research on alcohol preference to human alcoholism is rejected out of hand by some on the grounds that the measures of alcohol ingestion of the mice or rats did not at the same time assess all other aspects of addiction, particularly tissue tolerance and physical dependence. It is difficult to account for this requirement of complete isomorphism of the animal model to the human situation in the case of behavioral traits. In other scientific contexts it seems to be agreed generally that simplification is often a useful precondition for understanding of complex phenomena. A complete model would be desirable, without doubt, but it is not obvious that partial models will not shed important light. Again, it would seem to be an empirical question for any particular trait. The proof of the model will be in its application, and it is likely that we will discover that some models are extremely useful and that others are worthless.

Alexander Pope may have been correct in asserting that the proper study of mankind is man. In some cases, however, we may advance this study most rapidly by an apparent detour through research on his phyletic relatives.

ANIMAL BEHAVIORAL GENETICS

A major practical reason for using infrahuman animals in genetics research is that mating can be controlled. Species of choice tend to be those that have large numbers of progeny and short generation intervals. An additional requirement for behavioral genetics research is that the animal display some behavior of interest. "Interest" is, of course, largely in the eye of the beholder, but there has been a strong tendency to deal with behavior related to central issues within Psychology.

The compromises over these sometimes conflicting desiderata have given rise to research that has concentrated on a few species, with most of the work involving Drosophila, mouse or rat. The breeding procedures have variously involved selective breeding, crossing of inbred strains, and to a lesser extent random mating, with study of correlations among relatives and techniques appropriate to single locus analysis. The behaviors have included geotaxis, phototaxis, activity, hoarding, sexual behavior, social dominance and aggression, emotionality, alcohol preference and audiogenic seizures. The basic fact that there is some genetic influence on the trait has been clearly demonstrated for all of these. A few years ago, this simple demonstration was regarded as noteworthy, because a long tradition of exclusive environmentalism was being challenged within Psychology. The success of efforts to demonstrate a genetic component has been so consistent that it is now a foregone conclusion, and efforts have been largely directed to quantitative analysis or to analysis of the physiological mechanisms. The different phenotypes have lent themselves differentially to these enterprises. The behavioral domain of activity has been particularly amenable to quantitative genetic analysis, for example, and a large number of papers have been published in this area. Audiogenic seizures, as another example, have been particularly useful in the search for neurochemical bases of the influence of the genes. Overall, the results of these studies lead to the conclusion that the domain of behavioral phenotypes is not particularly unique, and that no rules of inheritance other than those described for non-behavioral characters need be invoked to account for their transmission.

The growth of the field of animal behavioral genetics has been very robust in recent years, and the total literature now is too extensive for review here. Recent reviews elsewhere may be consulted for overviews (Lindzey, Loehlin, Manosevitz and Thiessen, 1971; McClearn, 1970). For present purposes, the methodologies employed and the type of evidence adduced may be summarized by the work in one behavioral area. Because learning has often been placed in an antithetical position with respect to "native" traits, it seems particularly appropriate to examine the data on the inheritance of the learning process itself.

GENETICS OF LEARNING

Learning was one of the earliest foci of interest of behavioral genetics. Because the rat had early become established as the "standard" psychological research animal, it is natural that the earliest work made use of this animal. Tolman's (1924) pioneering selective breeding program for rat maze-learning served as a pilot study for Tryon's (1940) classical work on "maze-brightness" and "maze-dullness." This work was paralleled by that of Heron (1941) who was also successful in breeding selectively for rat learning performance in a different type of maze. Other more recent selection studies have included Thompson's (1954) work with the Hebb-Williams maze, which may be superior as a model of human "intelligence" because of its graded difficulty, and Bignami's (1965) study which dealt with avoidance learning rather than appetitive learning.

The mouse had low popularity as a behavioral research animal, but became well studied genetically. The growing interest in the genetics of mouse learning has most often been expressed in strain comparison work, as contrasted with selective breeding in rats, perhaps because of the availability of a large number of highly inbred mouse strains. Rather surprisingly, in view of the quantitative distribution of learning in these studies, there has been relatively little effort expended upon classical quantitative genetic analysis. Most of the research can be subsumed under the rubric of a search for "correlated characters." Sometimes these researches have been oriented towards other characters also at a behavioral level of analysis; sometimes they have reflected a reductionist orientation, and have sought to relate differences in learning performance to physiological properties.

One of the earliest concerns was to determine the generality of the difference between selected lines. Searle (1949), for example, administered a series of learning tasks to a sample of Tryon maze-bright and maze-dull rats. One finding was that on some learning tasks, specifically escape from water, "maze-dull" animals were brighter than "maze-brights." Tryon himself had been very explicit about the fact that his selection was for a particular phenotype, operationally defined as the number of errors in his particular maze. This point was not always understood, however, and the failure of the maze-brights and maze-dulls to be universally bright and dull was interpreted by some, who didn't much understand or like the idea anyway, as weakening the argument that genes could influence learning ability at all.

In a similar vein, the generality of differences in learning performance among inbred strains of mice has been explored. McClearn (1958, 1961) found C3H mice to be poorer performers than C57BL or BALB/c mice in an elevated maze, a visual discrimination apparatus, and a tactual discrimination apparatus. Bovet, Bovet-Nitti and Oliverio (1969) found striking strain differences in both shuttle box avoidance learning and Lashley III maze learning. A general consistency was found across situations, with those strains performing well in one apparatus also performing relatively well in the other. Among the strains tested was the C3H strain, and animals of this group proved to be inferior to C57BL, BALB/c, DBA/2 and several others. These investigators were also successful in selectively breeding for the shuttle box behavior, beginning with a foundation population of genetically heterogeneous Swiss mice. Lindzey and Winston (1962), using a 6-unit multiple T-maze, also found C3H animals to be relatively inferior to C57BL, DBA and A mice. C3H's performed less well than C57BL and BALB/c in a wheel turn shock avoidance apparatus (Zerbolio, 1967), and were only mediocre in a jump box shock avoidance situation (Schlesinger and Wimer, 1967). Winston (1963) again found C3H's to be inferior to A and DBA animals in an enclosed maze, but superior to them in a water-escape situation. C3H mice have also been found to perform relatively well in another water-escape study (Winston and Lindzey, 1964) and in shuttle box avoidance situations (Bovet and Oliverio, 1967; Carran, Yeudall and Royce, 1964; Collins, 1964; Royce and Covington, 1960).

These results testify to the complexity of the phenotypic category of learning performance. One way of exploring this complexity has been the examination of what might be regarded to be components of the performance. Krechevsky (1933), for example, tested some of Tryon's strains in an apparatus that permitted analysis of an animal's performance in terms of responsiveness to visual and spatial cues. He found that the "maze-bright" rats employed more spatial "hypotheses" and the "maze-dull" used more visual "hypotheses." This result is, of course, consistent with the fact that the maze employed in the selection study was enclosed and therefore offered minimal visual stimuli pertinent to the correct choice.

Heron and Skinner (1940) reasoned that since error reduction is the elimination of incorrect responses, animals differing in maze learning ability should differ also in rates of extinction in a bar-press situation. When tested on Heron maze-bright and maze-dull rats, however, this expectation was not confirmed. Another exploration of the nature of the difference between Heron's bright and dull animals was undertaken by Harris (1940). The maze used by Heron permitted scoring of two types of error: first errors, and repeat errors at each of the successive choice points. In examining the error scores over trials, typical learning curves were found for both strains, with the error curve of the dulls being, of course, higher than that of the brights. Closer examination revealed that both types of error were reduced in the learning performance of the brights, but only the repeat errors were reduced by the dulls. That is to say, the dull rats' learning consisted solely of learning not to repeat a mistake once made; they learned essentially nothing about correct initial responses at the choice points.

The matter of different error types was explored in detail by Wherry (1941), who analyzed some of Tryon's original data in terms of a forward-going error producing factor, a food-pointing factor, and a goal gradient factor. The relative importance of the forward-going factor declines over trials in a similar manner in both strains. The goal gradient factor rises in both, but more rapidly and to a higher relative level in the maze-bright strain. The food-pointing factor, which begins at a moderate level and subsequently declines in the brights, begins at a low level and rises rapidly to become the predominant factor in the latter trial performance of dull animals.

More recently, McGaugh and colleagues (McGaugh, Jennings and Thomson, 1962; McGaugh and Cole, 1965) have studied the influence of distribution of practice on the behavioral differences between descendents of the Tryon maze-bright rats (now called S-1's) and maze-dull rats (S-3's). This particular parameter of the learning situation is a central one, because it is related to the consolidation of memory traces. Briefly stated, strain differences in the expected direction were found in performance in a Lashley III maze when a 30-second interval was provided between trials, but no differences were found with intervals of 5 minutes, 30 minutes or 24 hours. Age of the animals has also been found to affect the strain difference in response to distribution of practice. These results clearly imply genetically influenced differences in rates of neural consolidation.

Genetic differences in response to inter-trial interval have also been found in mouse research. In one study (Wimer, 19) both the active shock escape learning and passive shock avoidance learning of C57BL mice were betterunder a long (24-hour) inter-trial interval condition than with brief (5-40 second) intervals; for DBA/2 mice, the converse was true. Another mouse study on distribution of practice has yielded strain differences (Bovet, Bovet-Nitti and Oliverio, 1968). In shuttle box avoidance learning, 500 trials were presented either in one continuous 250-minute session or in five 50-minute sessions at daily intervals. The distribution of practice over five days resulted in a dramatic enhancement of learning compared to the continuous session performance in DBA/2 mice, but resulted in poorer performance in C3H and BALB/c mice. Similar strain differences were found in continuous sessions when the inter-trial interval was either 30 seconds or 120 seconds. These results for DBA/2 mice appear inconsistent with those described in the preceding study (although differences did exist in apparatus and tasks), and further study obviously is required to sort out the matter. Nevertheless, these demonstrations of strain differences have amply shown a genetic influence on memory and consolidation mechanisms.

A rather different approach to the inheritance of mouse learning was taken early by Vicari (1929). In time scores on a maze learning task, she found several inbred strains to be characterized by one of three types of learning curve: a flat curve, a classical descending curve, and a descending-ascending curve. Results from F1's and F2's suggested dominance for the alleles influencing faster response time, and there was even some evidence that only a single locus might be involved in the difference between the flat curve and the classical one.

In relating strain differences in learning to physiological systems and events, it has been natural to look to the nervous system. Rosenzweig, Krech and Bennett (1960) have described results of a major program seeking to discover neurochemical bases of the behavioral difference between the S-1 and S-3 Tryon strain descendents. They hypothesized that the differences in learning performance are related to neural efficiency and that neural efficiency is related to the biochemistry of the neurotransmitter, acetylcholine. The first investigations dealt with the enzyme acetylcholinesterase, and results were in accord with a straightforward hypothesis: S-1 rats had more acetylcholinesterase than did S-3 rats. As part of the same overall program, Roderick (1960) began selective breeding from a heterogeneous foundation population of rats for levels of the enzyme; after lines were satisfactorily separated on this measure, they were tested for learning ability. The results did not confirm the earlier ones; the high enzyme strains were generally inferior to the low enzyme strains in performance. Subsequent work has led to the position that the ratio of the substrate, acetylcholine, to the enzyme acetylcholinesterase is consistently related to learning in all of the rat strains tested. Other recent work by Schlesinger and his colleagues (see Schlesinger and Griek, 1970) has explored the genetics of the neurotransmitters serotonin, norepinephrine and gamma-aminobutyric acid in the context of seizure susceptibility.

The work just briefly reviewed has followed the basic tactic of observing trait B in two or more strains already discovered (in the case of inbred strains) or bred (in the case of selected strains) to differ with respect to trait A. Useful as this procedure is in generating hypotheses or in their initial testing, it suffers from shortcomings, as well. Given a difference in trait A between two strains, there are three possibilities with respect to any other trait B: the high-A strain may also be significantly higher on B than is the low-A strain; it may be significantly lower; or it may not differ significantly. The latter outcome is quite strong information, allowing the rejection of an hypothesis that traits A and B are related. A significant mean difference in B contrary to the hypothesized direction would also permit rejection of the initial hypothesis and would probably prompt some intellectual gymnastics. Unfortunately, an outcome confirming an hypothesis is extremely weak in these circumstances. The differences in trait B might be entirely fortuitous, reflecting no causal connection at all between A and B, but only chance fixation of alleles.

A solution to this difficulty is very straightforward. One need only examine the correlation between A and B in a segregating population. If A and B share no loci, then segregation should yield a phenotypic correlation of zero. If there are shared genes, a correlation will be expected. One appropriate segregating population for tests of this sort is an F2 or subsequent generation derived from an F1 between the two parent strains. The possibility of linkage can complicate interpretations of F2 data somewhat, although subsequent generations should clarify the issue with respect to all but very closely linked loci.

Populations with greater genetic heterogeneity than F2's also provide useful animals for examining associations between traits. An example pertinent to the topic of learning is provided by Tyler and McClearn (1970) who studied straight runway learning in a parent and offspring generation of HS mice. This stock was established by crossing of eight inbred strains, and is maintained by systematic matings which minimize inbreeding. A polynomial of the simple form $Y = a + bX + cX^2$, where Y is in terms of running time and X is number of trials, was fitted to each animal's acquisition record. Separate estimates of heritability were then determined for a, b and c. These ranged from 0.19 to 0.40. Examination of the genetic correlations of various indices of acquisition and extinction led to the conclusion that the genes influencing the initial part of acquisition performance contribute less to performance as learning progresses, but come into play once again during the later parts of the extinction process.

Another way of dealing with association between traits presents itself when one of the traits is already known to be inherited in a simple fashion. In learning phenomena this situation arose with respect to the albino locus. A simple observation that animals of an albino inbred strain perform more poorly than do those from a pigmented strain is subject to the limitations cited above: The behavioral difference may be due to thousands of loci other than the albino locus. Indeed, the _a priori_ odds would seem to be quite long against an association with any particular locus such as this which is singled out largely because its phenotypic effect is obvious. Clearly, the association can be put to the test in a segregating population. Winston and Lindzey (1964) found that albino segregants in an F2 between the albino A strain and the pigmented DBA strain were poorer in water escape learning than their pigmented littermates. Further work (Winston, Lindzey and Connor, 1967) showed differences in response style also to be associated with the albino locus in that albino segregants employed passive avoidance almost exclusively, whereas pigmented animals used both passive and active avoidance about equally.

It is true, of course, that the F2 data cannot rule out a locus linked to the albino locus as the responsible agent. The data of Tyler (1970) on HS animals in which a number of segregating generations had occurred is confirmatory, however. His albino segregants were inferior in straight runway learning to their pigmented controls. Even more persuasive, however, is the evidence from animals in which a mutation to the recessive allele for albinism has occurred on a pigmented inbred strain background. In this case, the albino animals are presumably like their pigmented strain mates at all loci other than the albino locus, and any differences in behavior can be clearly ascribed to that locus alone. Fuller (1967) and Henry and Schlesinger (1967) employed a stock of C57BL mice in which such a mutation had occurred. They were able to show inferiority in performance of the albinos in a water escape and in a shock avoidance situation, respectively.

In concluding this brief review of the animal learning literature, it may be said that these studies have clearly demonstrated an hereditary basis for learning performance of several kinds in mice and rats, and have also shown the utility of genetic techniques in analyzing traits correlated with, and mechanisms underlying, learning behavior.

SUMMARY AND CONCLUSIONS

Overall, we might ask, what has the animal behavioral genetics literature contributed to knowledge? It seems to me that a general contribution has been in demonstrating, in company with human data, the plausibility of the modern genetic perspective in application to the realm of behavior, and helping thereby to lay to rest the old nature-nurture formulation. In itself this would represent a reasonable accomplishment, since this dichotomous view still is a formidable barrier between parts of the social sciences and the biological sciences.

As a corollary, the animal data have helped to provide a new perspective on individuality. Lamentably, many social science formulations would have it that the only source of variability is environmental, and that we all start life essentially as uniform, interchangeable biological units, devoid of individuality. The genetic view of variability as a biological necessity, and an appreciation of the mechanisms that assure it, add a whole dimension of explanatory power to a simple environmental model, and permit the analysis to consider interactive effects between environmental factors and the biological uniqueness of the individual. Such perspective should be particularly valuable in respect to the educational process.

Finally, the animal behavioral genetics literature has strong implications of a pragmatic sort for the conduct of animal behavioral research in general. The genotype dependence of so many effects, even, as we have seen, such "robust" effects as those of distribution of practice, is a clear warning about the generalizability of results obtained on genetically unspecified animal subjects. Replicability, that *sine qua non* of a science, suffers when research is conducted on the nondescript groups used by so many contemporary researchers, and thus the cumulative build up of knowledge that is supposed to characterize a science is severely impaired. The use of genes as variables, to be held constant by choice of a single strain for investigation; to be manipulated as fixed effects by making strain comparisons; to be manipulated by selective breeding; or to "randomize" by use of a deliberately genetically heterogeneous stock, can increase research efficiency greatly.

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HUMAN BEHAVIORAL GENETICS

by

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HUMAN BEHAVIORAL GENETICS

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The population geneticist tries to make mathematics serve biology. The behavioral geneticist tries to make biology serve psychology. My training and interests prevent me from exploring this possible conflict, and I shall restrict my discussion to the use of mathematics to answer certain biological questions about human behavior.

1. What are the effects of single genes on behavior?

The rationale for single gene studies was given by Thiessen et al. (1970): "The beauty of single gene analyses lies in the possibility of tracing the physiologic interactions from the initial gene alteration to the behavior in question. The alleles can be easily identified, manipulated as independent variables, and, in several cases, related to known metabolic pathways. It is as if only one letter of a word is allowed to vary at a time in order to study its special influence."

As in the mouse and Drosophila, many neurological mutants are known in man with gross effects on behavior, and probably a large fraction of other mutants modify behavior more discreetly. Considering that the academic interest of this material is reinforced by immediate prospects for better management of disease, surprisingly little research has been directed toward characterizing these effects, especially the more subtle and specific carrier signs. Some mutants, like total albinism, are similar to (and may be homologous with) genes in the mouse with known effects on behavior (including activity level and alcohol preference in the case of albinism). It is an interesting problem whether these effects are similar in mouse and man. Do the behavioral manifestations of phenylketonuria in homozygotes and carriers correspond to its dietary phenocopy in mammals? Answers to questions such as these would establish the comparability of human and mammalian behavior tests: for example, does alcohol preference in the mouse correspond to any behavioral trait in man (Henry and Schlesinger, 1967)?

The experimental design for such studies is extremely simple. Let

$$\begin{aligned} Y &= 1 \text{ for a genotype to be tested} \\ &= 0 \text{ for a control genotype} \end{aligned}$$

and let X_i be the score on the i^{th} test. Then the stepwise regression of Y on the X_i identifies tests which discriminate between the genotype and its control and assigns these tests efficient weights. If desired, some of the X_i may represent psychological factors defined as linear function of the scores, in which case the regression provides a test of whether the factors are efficient discriminants of genetic differences. If the controls are paired, the regression may be performed within pairs.

One objective of such studies might be to select a battery of mutants which, in their characteristic expression or more subtly in carriers, have highly specific behavioral effects. This would lead to an inversion of the current procedures for test validation: instead of circularly correlating a new test with old ones which are presumably better characterized, the test would be screened for its ability to differentiate a selected battery of genotypes.

The intraclass correlation for the discriminant is a measure of the behavioral effect relative to the unitary genetic difference: it may be called the heritance of the behavioral effect. Such an index of genetic determination of behavior is much more specific than the heritability defined on the general population, and its estimation is not fraught with any serious problems. If there remain psychologists who believe that behavior has no genetic component except at the neuropathological limit, and if such a position requires any answer but the mortality table, the heritance of single gene effects may be an appropriate rebuttal, since it simultaneously tests for a behavioral effect of a genotype recognized by other criteria and measures the strength of genetic determination.

A similar approach can be applied to relatives of probands for complexly inherited traits, like schizophrenia, to detect a possible carrier state, using the coefficient of relationship as dependent variable. The likelihood of heterogeneity is greater than for recognized single gene traits.

There have been several attempts to detect behavioral effects of polymorphisms. Cohen and Thomas (1962) reported an excess of blood groups B and AB in nonsmokers or occasional smokers. Cattell et al. (1964) found an association between tender-mindedness and blood group A in tests of 14 personality factors. Parker et al. (1961) reported an excess of group O among manic-depressives, which was not confirmed by Tanna and Winokur (1968). The other claims seem not to have beem retested, and the evidence is far from convincing. A clear association between duodenal ulcers, group O, and ABH non-secretors has been shown, with no indication that it is psychologically mediated (Roberts, 1959). The latter studies have used sib controls and (with much greater power) tests of association within ethnic groups as replicates to avoid stratification errors.

2. What are the effects of chromosome aberrations on behavior?

As with single genes, little use has been made of chromosome aberrations in human behavioral genetics, the principal exception being the work of Shaffer (1962) and Money (1963) on specific space-form perception deficit in Turner's syndrome (both chromatin-positive and chromatin-negative). This suggests many questions; for example, do XO mice share this specific deficit? If so, homologous tests of space-form perception are thereby defined in the two species. Do XXX females differ in the opposite direction, in analogy with Lejeune's concept of anti-trisomy? Are the defects developed before puberty, when hormonal infantilism and dwarfness complicate the picture? Are the behavioral effects of sex chromosome aneuploidy large by comparison (through the intraclass correlations) with effects on finger-ridge count, an almost perfectly heritable trait?

XXY and XYY males are prone to various psychological dysfunctions, which are poorly defined. Does the chromatin-negative Klinefelter share XXY behavior? Does the XXY tortoise-shell cat show homologous disturbances? Are the mental deficiency and schizophrenia occasionally associated with XXY of a specific type? What is the role of an extra Y in anti-social behavior, and how is that behavior characterized?

Many autosomal aberrations have gross effects on behavior by comparison with the X-chromosome anomalies, which rarely fall in the psychopathological range. However, even in the case of Down's syndrome (trisomy-21), mosaics and partial trisomics provide nearly normal material for study. Recent improvements in autoradiography detect small deletions.

duplications, and inversions, and offer the hope of localizing genes which alter behavior without a comcomitant morphological effect.

The method of discriminating behavioral correlates is the same as for single genes, and the same measure of heritance applies.

3. How can behavior whose transmission is unknown be screened for sensitivity to genetic differences?

This question is the most difficult so far, and the theoretical and practical importance of an answer is less obvious, but it has attracted much attention as the "nature-nurture controversy". The alternative of investigating heritance of behavior for simple genetic differences should be considered.

Another possibility is to concentrate on predominantly environmental factors, such as regional school expenditure per child (Spuhler and Lindzey, 1967), parental income, and parental socioeconomic status. After allowing for test unreliability, the behavioral traits most sensitive to these effects (measured as a multiple correlation) may be least sensitive to genetic differences, but the possibility of gene-environment covariance makes quantitation suspect.

Since environmental effects on behavior are complex, the genetic model should be simple if it is to be of any use. Dominance, epistasis, and the genetic component of assortative mating must be neglected as unmeasurable where environment is not randomized. The test of Fisher and Gray (1938) provides some check on these simplifying assumptions. Let Y be a score for individual behavior, X be the midparent score, and Z be the product of maternal and paternal scores. Then the regression

$$Y = a + bX + cZ$$

provides a test of the hypothesis that $c = 0$, in which case certain non-additive effects (both genetic and environmental) are negligible. Of course this test does not detect all deviations from additivity, but it is the only method applicable to nonexperimental data. Note that it may be used for interracial crosses.

Gene-environment interactions are best studied by comparisons of relatives living together and apart. If each genotype selects its environment in a characteristic way, the more closely related are the members of a pair, the less will be the effect of separating them. For example, Berry et al. (1955) and Gartler et al. (1955) noted that the amino acid excretion pattern of identical twins was less affected by separation than the pattern of fraternal twins, and suggested that identical genotypes select similar diets and environments (Table 1). If this is a general phenomenon, as suggested for domestic animals by Robertson (1950), the limits of behavioral genetics are wide indeed: one would not ordinarily consider amino acid excretion a behavioral trait. Gene-environment interactions of this selective type vitiate heritability studies. More attention should be directed to them. Note that the members of the pair need not be separated for long periods of time, it being sufficient to compare performance together and separately.

Another kind of interaction has been reported in the aussenvertreter effect, whereby identical twins take opposite roles (Woodward, 1941), increasing the within-pair and total variances. Eysenck and Prell (1951) have published data on neuroticism score which indicate that single monozygous twins are more variable than dizygous twins, due to an increase in the among-pair variances (Table 2). This large difference renders meaningless the comparison of intraclass correlations and calculations of heritability. One wonders if their result is repeatable: other workers have not noticed such an effect.

Cattell (1953) has developed models for relatives reared together and apart in terms of genotype-environment correlations, interactions being ignored. Formally such a correlation is equivalent to shared environment, and it simplifies the notation to so consider it.

As an illustration of these principles, consider a trait Y measured on various relatives subjected to different commonness of environment. It is convenient to array the data as for the old method for calculating an intraclass correlation (Fisher, 1950, p. 214), each measured group of k relatives generating k (k-1) ordered pairs. Let Y_1 be the first member of such a pair and Y_2 the second member, let R be the coefficient of relationship, let S be a vector of non-genetic variables (like age, income, socio-economic status) whose linear effects are to be eliminated, and let C be a vector of common environment. For example, we might take

C_1 = 1 for individuals reared in the same household, as sibs or parent-offspring
= 0 otherwise

C_2 = 1 for twins reared together
= 0 otherwise

C_3 = 1 for individuals reared in the same household as parent-offspring
= 0 otherwise

Then the regression

$$Y = a + \Sigma b_i S_i + \Sigma b_j C_j + BR$$

yields an adjusted variate

$$Y' = Y - \Sigma b_i (S_i - \overline{S}_i) - \Sigma b_j (C_j - \overline{C}_j) - B(R - \overline{R})$$

from which the linear effects of the S_i, C, and R variables have been eliminated. Let us suppose that this is done for Y_1 and Y_2, using the coefficients calculated from the former (in which each member of a group of k relatives is repeated k - 1 times). We may also correct Y for attenuation (i.e., test unreliability), but there seems little point in this.

The regression

$$\ln \left[(Y' - \overline{Y})^2 \right] = a + \Sigma b_i S_i + \Sigma b_j C_j + BR$$

tests for differences in variance among groups. Only in the absence of such differences can the analysis proceed, and so the data must be partitioned into sets with homogeneous variance.

Assuming that this has been done, we make the regression

$$(Y'_1 - Y'_2)^2 = A + \Sigma b_j C_j + BR$$

Under the model the heritability is

$$h^2 = B/A$$

and for values of b_j significantly different from zero the ratio b_j/A is the fraction of variance due to the j^{th} type of common environment. The remaining fraction $1 - \left[\frac{B + \Sigma b_j}{A} \right]$ of the variation is due to unexplained environmental differences, errors of measurement, and interactions.

Data are almost never reported in a way suitable for this kind of analysis. Usually only the intraclass correlations are given, not adjusted for S variables. On the doubtful assumption that variances are the same for all groups, we may make the regression

$$\rho = A + \Sigma b_j C_j + BR$$

where ρ is an intraclass correlation which may be weighted by the number of observations. Then $E(A) = 0$, and the heritability is $h^2 = B$, the significant values of b_j estimating the fraction of variance due to the j^{th} type of common environment. The fraction $1 - B - \Sigma b_j$ of the variation is due to unexplained environmental causes.

As an illustration of this approach, it has been applied to median correlations reported by Erlenmeyer-Kimling and Jarvik (1963) from a literature survey of intelligence tests (Table 3). Weighting by the number of studies we find that

h^2 = .675, due to genetic differences
C_1 = .139, due to common environment
C_2 = .016, due to common environment specific for twins
C_3 = 0, the difference between common environment of sibs and children
residual = .170, due to random environment

Errors of measurement due to unreliability of the tests depress h^2 by an amount which can be calculated. Other errors are irreparable, stemming mostly from failure to characterize relevant common environment. Thus twins or sibs reared apart share prenatal and some part of the postnatal environment, which tend to overestimate h^2. It is sometimes stated that arteriovenous anastomosis and mirror-imaging in monozygous twins depress heritability, without noticing that such an effect must increase the variance of single twins. If no such increase is detected, no claim of underestimation should be made. The selective type of gene-environment interaction, whereby close relatives choose similar environments, raises a philosophical problem. If such interactions are important, they ten to overestimate h^2 unless we wish to include the selected environment as heritable in some casuistic sense.

My conclusion is that measures of heritability when the environment is not randomized are fraught with uncontrollable difficulties. Instead of asking the geneticist to develop a better method of estimation, the psychologist should perhaps reconsider his reasons for wanting to estimate heritability when no selection experiment is envisaged.

Before leaving this subject, I would like to recall the most careful analysis yet performed, an exercise in path coefficients by Sewall Wright (1931) which seems unknown to behavioral geneticists. Barbara Burks (1928) in her classical study of foster children had applied path coefficients to correlations corrected for attenuation, and had concluded that heritability of general intelligence is .75 to .80. Wright pointed out that her model (Figure 1) is genetically unacceptable, since both parental I.Q. and child's I.Q. are resultants of parental genotype and environment. To develop a better model he had to make a number of assumptions, as follows:

1. the environment relevant to general intelligence is perfectly measured by a score for material and cultural advantages of the home
2. dominance and epistasis are negligible
3. heredity and environment are additive
4. the ratio of residual to genetic determination is the same for parents and children, but environmental determination is greater for parents

5. the correlation between midparental and child's genotype, allowing for assortative mating, is .78 (where .71 would be expected under panmixia)

Psychologists may be surprised that Wright made the first assumption more lightly than the second. His solution is given in Figure 2. The heritability is $.71^2 = .50$ for children and $.56^2 = .31$ for parents, but this includes home environment not measured by the score for material and cultural advantages of the home. Essentially the same estimate is obtained much more simply from the values for sibs and foster sibs in Table 3:

$$h^2 = 2(.49 - .23) = .52$$

which is less than the estimate from monozygous and dizygous reared together:

$$h^2 \doteq 2(\rho_{mz} - \rho_{dz}) = 2(.87 - .53) = .68$$

The first estimate assumes that environment is as similar for foster sibs as for genetic sibs, the second estimate assumes that environment is as similar for dizygous as for monozygous twins. Both assumptions are probably false, and so the heritability of general intelligence may well be less than any estimate so far made.

Twin researchers often use Holzinger's measure of heritance,

$$H = \frac{\rho_{mz} - \rho_{dz}}{1 - \rho_{dz}}$$

which is sometimes miscalled heritability. From Table 1 we see that a simple assumption is

$$\rho_{mz} = h^2 + T$$

$$\rho_{dz} = h^2/2 + T$$

where T is the environment common to twins. Thus

$$H = \frac{h^2}{2 - h^2 - 2T}$$

and so

H is greater or less than h^2 according as T is greater or less than $\frac{1 - h^2}{2}$. This confusing statistic has no merit, since on the same doubtful assumptions

$$h^2 = 2(\rho_{mz} - \rho_{dz})$$

If I understand the present state of behavioral genetics, the phase of trying to convince skeptics that behavior is in some degree heritable has now ended. In any case, no intelligent skeptic would be converted by a heritability estimate, which a geneticist finds unconvincing. Good indices of heritability comes from single gene traits, chromosomal aberrations, animal experiments, and the experience of biometrical genetics that a trait heritable at its extremes has never been found to have zero heritability within the normal range.

The usefulness of heritability estimates in man seems therefore limited to selection of heritable traits for further study. For this point the criterion

$$2(\rho_{mz} - \rho_{dz})$$

is satisfactory, even if the assumptions on which it is an estimate of heritability are questionable.

Parenthetically Bartlett (1951) showed how to maximize an intraclass correlation. The same method can be used to maximize ρ_{mz}/ρ_{dz}, and hence heritability, but this seems less useful than to maximize discrimination of defined genotypes.

4. How can the inheritance of behavioral attributes be studied?

Traditional twin studies used for attributes the heritance

$$H = \frac{C_{mz} - C_{dz}}{1 - C_{dz}}$$

where C_{mz}, C_{dz} are the concordances for monozygous and dizygous twins, respectively. Concordance is defined as the probability that the co-twin of a twin proband be affected, and can be conveniently estimated by the Weinberg formula:

$$C = \frac{\text{number of twin probands with affected co-twins}}{\text{number of twin probands}}$$

No precise genetic meaning is attached to this measure of heritance.

Recently two other approaches have been made to the inheritance of attributes. One is the generalized two-allele single-locus model, according to which the risk for affection is z, z+td, and z+t in the genotypes

GG, GG, and G'G', respectively. If A is the population incidence, and $z \ll t$, then $x = z/A$ is the proportion of cases which are sporadic: i.e., seldom recurrent in sibships (Morton et al., 1971).

Such a model, while seemingly restrictive, is actually so flexible as to be difficult to exclude. Given the population incidence, there are 7 hypotheses of rank 1 (with one parameter estimated from the data):

no phenocopies, GG completely penetrant	($x = 0$, $t = 1$)
G dominant, completely penetrant	($d = 1$, $t = 1 - z$)
G additive, completely penetrant	($d = 1/2$, $t = 1 - z$)
no phenocopies, G additive	($d = 1/2$, $x = 0$)
G recessive, completely penetrant	($d = 0$, $t = 1 - z$)
no phenocopies, G recessive	($d = 0$, $x = 0$)
no phenocopies, G dominant	($d = 1$, $x = 0$)

Similarly, there are 5 hypotheses of rank 2:

no phenocopies	($x = 0$)
G dominant	($d = 1$)
G recessive	($d = 0$)
G additive	($d = 1/2$)
GG completely penetrant	($t = 1 - z$)

Commonly two or more hypotheses of the same rank fit about equally well, and so cannot be discriminated. Models with $d = 1/2$ are difficult to distinguish from additive polygenic inheritance.

An alternative model of rank 1 (given the incidence A) is quasi-continuous (Grüneberg, 1951). In the best derivation of this model (Smith, 1970), genes are assumed to act additively on a scale of genetic liability, which determines affection through a sigmoid risk function dependent on a single parameter, the heritability h^2 (Falconer, 1965).

Edwards (1967) presented an alternative model which allows the risk to increase experimentally beyond unity; despite this unreasonable assumption, the Falconer and Edwards models fit equally well to actual data. There are no significant advantages to Edwards' model, and Falconer's is more appealing.

All of these models for inheritance of attributes can be applied to pooled data on different degrees of relationship and, with more power, to segregating families (Morton, 1967; Morton et al., 1971). It turns out that a critical distinction in terms of likelihood ratio between quasi-continuity and the best single-locus hypothesis of rank 1 is difficult. Recessivity and a high ratio of recurrence risk to incidence favor the single-locus models. No case has yet been found where quasi-continuity fits much better than its single-locus alternatives of the same rank. Estimation of specific recurrence risks does not depend critically on the genetic model, a fact that should cheer genetic counselors and depress geneticists.

So far the modern methods of analysis have not been applied to behavioral attributes such as handedness, where inheritance is controversial. For the most critical test, data should be reported and analyzed by families, without pooling of sibships with different sizes and numbers of affected.

It is sometimes suggested that obscure and presumably complex traits like schizophrenia have been subjected to so much inconclusive genetic analysis that further investigation should be suspended until biochemical or other resolution is obtained. This point of view neglects the fact that recent advances in complex segregation analysis, which are capable of eliminating many genetic mechanisms, have not yet been applied to behavioral traits. Their utility should at least be explored before reaching a conclusion which may well be premature.

In application of these methods, it is desirable to define the liability by a discriminant function. For example, let

$Y = 1$ for an unaffected first degree relative of
a proband
$= 0$ for an unaffected control with no affected
first degree relative

and let X_i be the score on the i^{th} psychological, social, or biochemical variate thought to be relevant to the disease. Then the discriminant formed by regressing Y on the significant X_i can be studied by the methods of the preceding section to estimate heritability, and by the models outlined here if dichotomized into normal and abnormal. A followup study can determine a sigmoid risk function $Q(\hat{Y})$, where $\hat{Y} = \Sigma b_i X_i$ is the discriminant, and $0 < Q(\hat{Y}) < 1$ is the probability that an individual with score Y develop the disease in a specified time after testing. Then genetic analysis and counseling would both be reduced to the manageable problem of predicting the probability distribution of a continuous variable in relatives, given the distribution of liability in probands. Elston (1971) has suggested that pedigrees of three or more generations may provide the most powerful test of complex genetic hypotheses: such a test is better for a discriminant than for a rare disease.

5. Do psychological factors have genetic significance?

It is not obvious to a geneticist why precise discrimination of abnormalities has not played more of a role in behavioral genetics. Perhaps the reason is to be found in the traditional hold of factor analysis over psychologists, which seems to have arisen somewhat like this. Suppose two psychologists independently decide to study general intelligence, defined intuitively. For this they must compose a suitable battery of tests. Now imagine that their intuitions are similar with respect to most aspects of intelligence, and differ in one respect: the first notes that some idiots are tactile insensitive and includes a test of this in his battery, while the second considers this irrelevant. Then a factor analysis of the first battery will reveal a factor of tactile sensitivity absent from the second battery (cp. O'Connor and Hermelin, 1963). Clearly factor analysis can justly claim to reveal "vectors of the mind"--the mind of the person who composed the test battery. Whether tactile sensitivity is in fact an aspect of intelligence remains logically and operationally undefined, except by a discriminant function.

In recent years the development of admirable statistical methods and even more admirable computers has brought factor analysis within reach of everyone, obscuring the logical difficulties. Some psychologists have even supposed that the facets of performance identified as factors are in some sense unitary determinants of behavior. To a geneticist, accustomed to organelles and loci, this is incomprehensible simply because it is not mechanistic. A psychological factor cannot be a unitary determinant of

~~of~~ anything unless it resides in a specific organelle of macromolecule. However, we must not let our incredulity pass for knowledge. Many biologists felt just as incredulous about unit factors in genetics until they were shown to have a mechanistic basis. Much earlier, Socratic dialogues (the classical introspective analog of factor analysis) were enormously stimulating to philosophy if not to science.

The hypothesis that a linear function of variables, determined from a correlation matrix, is an optimum discriminant of a genetic difference is readily testable, as in the first section. There is no a priori reason why this should be the case, unless the binary dependent variable expressing the genetic difference were included in the matrix. Therefore criterion analysis, in which relations are sought between factors and diseases, seems merely an inefficient way to construct a discriminant function, unless the original data are simultaneously submitted to regression. The test of our question, "do psychological factors have genetic significance?", is so easy that someone should try it. Presumably the answer will be "yes, but not as much as ad hoc discriminants", which should replace factors as measures of behavior.

6. To what extent are group differences in behavior genetic?

Considerable popular interest attaches to such questions as "is one class or ethnic group innately superior to another on a particular test?" The reasons are entirely emotional, since such a difference, if established, would serve as no better guide to provision of educational and other facilities than an unpretentious assessment of phenotypic differences. Although without practical consequences, the question is interesting as a methodological problem which unfortunately remains unsolved. Assuming as the most economical hypothesis for correlations between relatives that intelligence is in some degree heritable, does it follow that a difference in performance on intelligence tests between two groups in different environments is also in some degree heritable? Obviously not, Jensen (1969) notwithstanding.

To study group differences, we may concentrate on environmental variables which differentiate the groups, and show that they account for at least a substantial fraction of the phenotypic difference. This requires two steps, in the first of which we discriminate between the groups in terms of environmental variables, to determine the most relevant set: and in the second we regress behavior on these variables *within* groups. Substituting the group means in this second regression, we predict the performance of each group in the absence of any genetic difference between them. Such an approach may show that a large fraction (perhaps all) of the observed difference is nongenetic, but it is subject to at least two criticisms: (1) some of the variation within groups may be due to correlations between environment and genotype, and to that extent the environmental part of the group difference will be overestimated; (2) the relevant environment cannot be perfectly measured, and to that extent the environmental part of the group difference will be underestimated, just as we suspect that the effect of home environment was underestimated when represented by a score for material and cultural advantages of the home in Burks' study discussed above.

An alternative approach is to look for members of the two groups, or of hybrids between them, living in the same environment. Maternal half-sibs living together offer the best material. Foster children are another possibility, but prenatal and early postnatal environment may be different between the groups. Interracial crosses usually involve considerable environmental similarity among hybrids of different constitution (F_1, B_1, B_2, etc.), the residual differences perhaps being small enough to be controlled by covariance analysis. A curvilinear relation between behavior and proportion of admixture could in principle be due to dominance, but could equally well indicate environmental effects. Thus Klineberg (1928) argued convincingly from intelligence tests in American Indians and mestizos, which by linear regression predicted a low I.Q. in pure Caucasians, that low performance in his material was social and not genetic. A final possibility is to abandon established differences in performance for differences in novel situations, like rate of learning of a new game, but perhaps this is no more culture-free than the so-called culture-free tests. Diallel crossing is more powerful if combined with covariance analysis of environmental differences. While group differences in a structured environment are messy for genetic analysis, promising methods exist which are almost never applied in behavioral genetics (Morton et al., 1967).

Studies of the decline of performance with inbreeding require painstaking controls from sibs or neighbors. Given these, or covariance analysis as a poor substitute, inbreeding depression can be used as an index of heritance (Schull and Neel, 1965). Such studies gain interest if combined with segregation analysis to determine whether rare recessive genes or increased variance of liability is responsible for the inbreeding effect (Adams and Neel, 1967).

7. What are the effects of behavior on population structure and selection?

Two important variables in population genetics are migration and selection, both of which are to greater or lesser extent behavioral. Migration clearly depends on topology, transportation, and political barriers: intense isolation by distance is found in Melanesians, where a boy who goes courting in the next village may lose his head (Friedlaender, 1971). It is not known whether genetic variability affects the tendency to migrate--such studies demand experimental material.

Closely related to migration are the customs of incest taboo and exogamy. Some anthropologists have speculated that group selection may have favored the incest taboo, which almost certainly arose and was promulgated for nongenetic reasons. I know of no experimental work on whether the tendency toward litter-exogamy is marked, and if so heritable.

There is a fascinating but uncollated literature on behavioral responses to single gene differences which could affect their fitness. The sanctity of albinos in the San Blas Indians probably increases their fertility. Deaf mutes tend to marry assortatively. Populations with thalassemia or hemoglobin S can occupy regions of hyperendemic malaria closed to unadapted groups. Consumption of fava beans may be contraindicated in a population with a high incidence of G6PD deficiency, and there is even a suggestion that the Pythagorean prohibition of beans stemmed from the susceptibility of G6PD deficient males to favism!

At a genetically more complex level, adaptations to extreme environments of heat, cold, and high altitude involve behavior as well as physiology. So far, it is unclear whether any of these adaptations are genetic, in the absence of the kinds of evidence on group differences discussed in the last section.

Going still further from simple genetics, polygamy of dominant males is a kind of phenotypic selection which may have some genetic basis. Are there genetic determinants of social dominance? One would suppose that heritability must be low for a trait subject to such intense selection. No genetic methods seem applicable to the primitive human populations where this question has been raised, and we must look to laboratory mammals for a critical study.

Summary

Available methods are discussed for answering 7 questions in human material:

1. What are the effects of single genes on behavior?
2. What are the effects of chromosome aberrations on behavior?
3. How can behavior whose transmission is unknown be screened for sensitivity to genetic differences?
4. How can the inheritance of behavioral attributes be studied?
5. Do psychological factors have genetic significance?
6. To what extent are group differences in behavior genetic?
7. What are the effects of behavior on population structure and selection?

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TABLE 1.

AVERAGE INTRA-PAIR VARIANCES FOR TWINS LIVING SEPARATELY AND TOGETHER

BERRY ET AL. (1955)

	Alanine	Glutamine	Glycine	Threonine
Dizygotics				
Separated	124.0	54.0	652.0	67.0
Separated (Excluding #37)	50.4	17.9	60.3	10.29
Together	9.7	5.0	22.5	9.3
Monozygotics				
Separated	21.8	21.0	42.4	1.9
Together	12.8	19.6	151.6	1.6

TABLE 2.

MEAN SQUARES OF NEUROTICISM SCORES

DATA OF EYSENCK AND PRELL (1951)

Source	Within pairs V_w	Among pairs $V_w + 2V_a$	Individuals $V_w + V_a$	Intraclass Correlation
Identical twins	13.68 (25)	172.67 (24)	93.18	.853
Like-sexed fraternal twins	32.48 (25)	50.83 (24)	41.66	.220

Number of degrees of freedom shown in parentheses.

TABLE 3.

INTRACLASS CORRELATIONS FOR GENERAL INTELLIGENCE

(Erlenmeyer - Kimling and Jarvik, 1963; after Spuhler and Lindzey, 1967)

Relationship	Number of Studies	Correlation ρ	Relationship R	Common Environment C_1	**Specific** Twin Common Environment C_2	Specific **Parent - Offspring** Common Environment C_3
Random pains	4	-.01	0	0	0	0
Foster sibs	5	+.23	0	1	0	0
Foster parent-child	3	+.20	0	1	0	1
True parent-child	12	+.50	.5	1	0	1
Sibs reared apart	2	+.42	.5	0	0	0
Sibs reared together	35	+.49	.5	1	0	0
DZ twins, opposite sex	9	+.53	.5	1	1	0
DZ twins, same sex	11	+.53	.5	1	1	0
MZ twins apart	4	+.75	1.0	0	1	0
MZ twins together	14	+.87	1.0	1	1	0

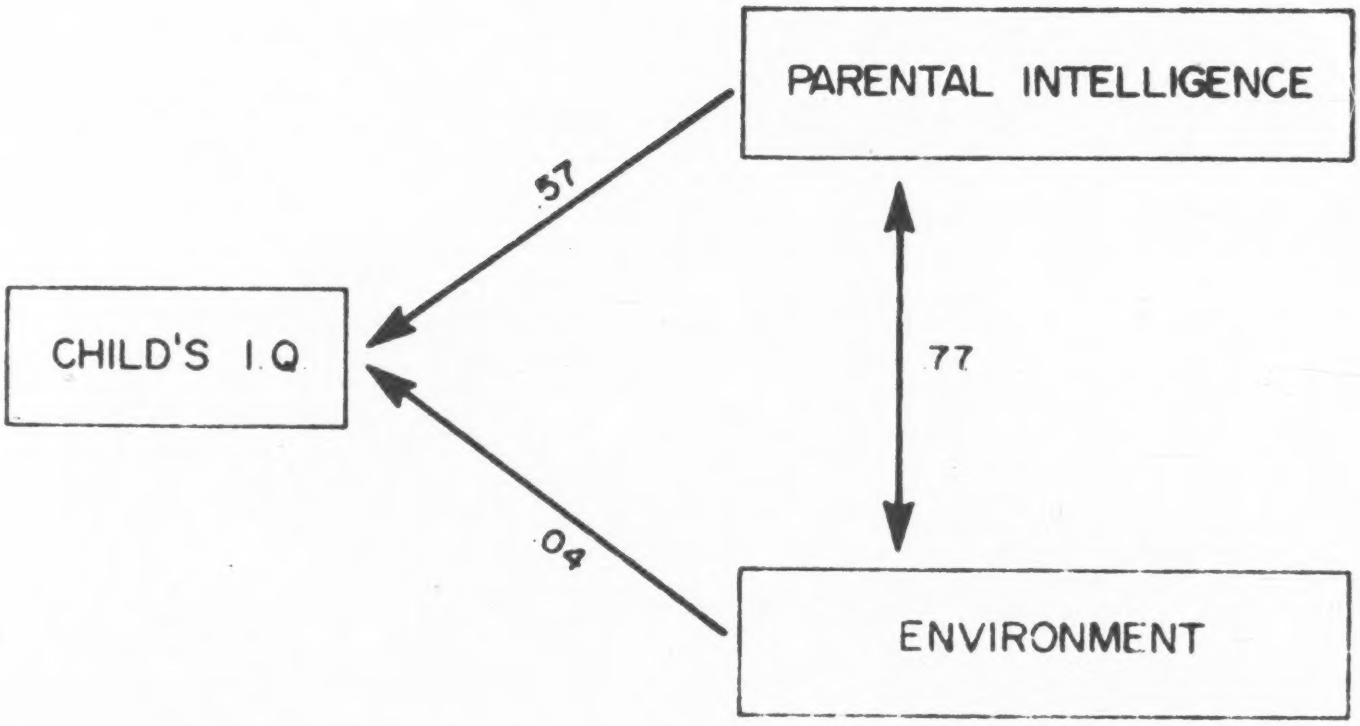
PARENTAL INTELLIGENCE
.57
CHILD'S I.Q
.77
.04
ENVIRONMENT

Figure 1. Burks' model for inheritance of intelligence

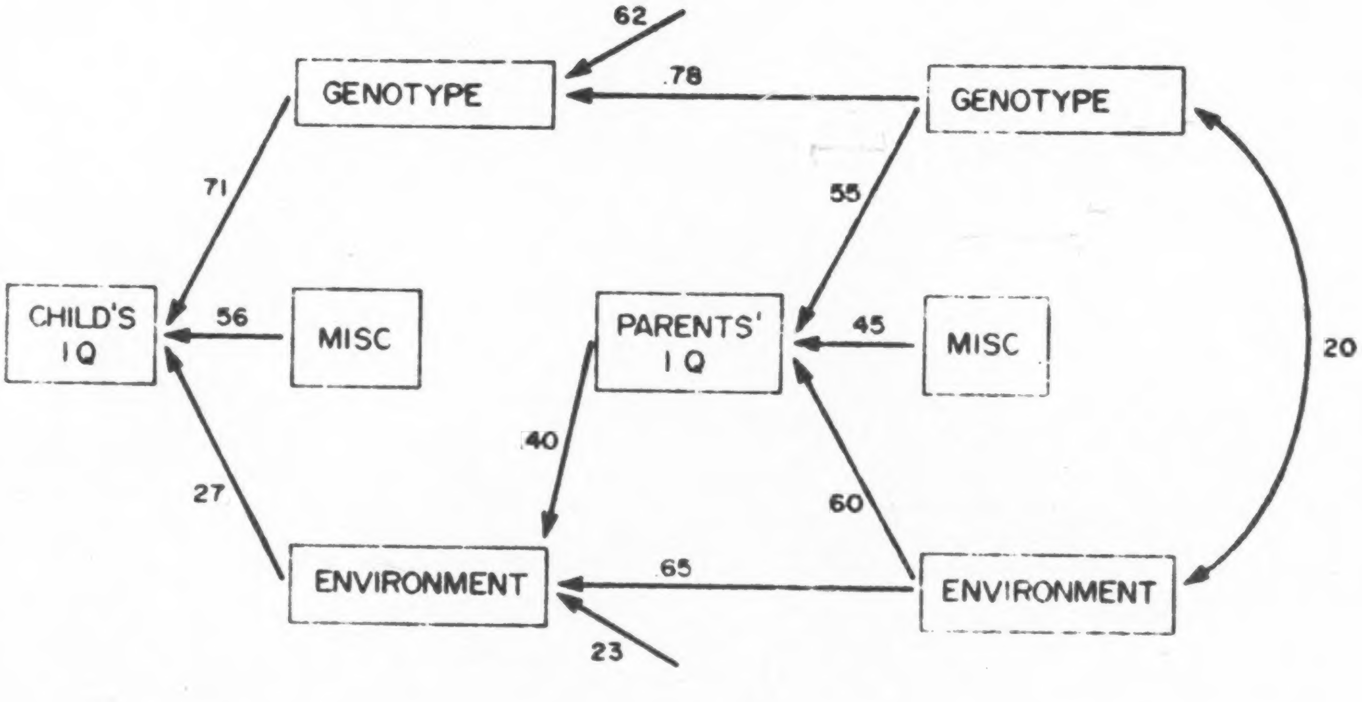
62
GENOTYPE
.78
GENOTYPE
71
55
CHILD'S IQ
56
MISC
PARENTS' IQ
45
MISC
20
.40
27
60
ENVIRONMENT
.65
ENVIRONMENT
23

Figure 2. Wright's interpretation of Burks' data

BIOCHEMICAL GENETICS
AND THE
EVOLUTION OF HUMAN BEHAVIOR

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A large body of evidence from animal models, twin studies, particularly of identical twins raised apart, and family studies points to a prominent role of genetic factors in behavioral phenotypes in man (1-6). The role of the genotype may be viewed first as one setting limits to nervous system function, the biological substrate for the range of normal behavior. In addition, abnormal genes predispose to or cause neurologic or psychiatric defects during fetal development and at various stages later in life. We have a strong faith in the generality of the mechanisms of gene action — that genetic information flows from the code of DNA via RNA messengers to protein products, with many regulatory steps affecting timing and magnitude of synthetic and degradative processes. All cells, including neurons and neuroglial cells, contain the same complement of DNA, but the regulatory processes of differentiation lead to different patterns of gene activation in different tissues. Evolutionary forces have acted on both the DNA complement and the processes of regulation. We have been assigned the formidable task of outlining the molecular basis of gene action, individual differences, and biochemical evolution and then trying to relate these biological processes to the structure and function of the human nervous system and to the evolution of human behavior.

We may ask what features of behavior are peculiarly human and cite language, upright posture, and increasing dependence on the technologies of our culture. Rensch (7) maintains that complex

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human behaviors involving abstract conceptualization and foresight represent only extensions of the capabilities of other animals. Although much may be inferred in man from knowledge of the evolution of the brain and behavior in other species, it is likely that certain features of human behavior can be understood only by the study of man.

Table 1 contrasts the features of biological and cultural evolution (10). Biological evolution depends upon chance occurrences of mutations in the genome and the selection by environmental forces of those few mutations that serve to enhance the viability or fertility of the species. It must be emphasized that selection acts on the whole individual (8,9), not just on specific genes. However, the example of the protective effect of sickle hemoglobin against malaria infection (11,12) demonstrates that selection can be based upon mutations at single loci. Cultural evolution proceeds at a pace many orders of magnitude faster than the biological processes. Cultural forces include social customs, which change over generations, as well as technological advances, whose impact may be felt in only a few years (see Table 2).

We will describe two complementary approaches in this discussion: 1) reductionist analysis of brain function at many levels, with emphasis on features especially worthy of comparative study; and 2) an effort to integrate behavioral and cultural features of man in the evolutionary context. The hopelessness of understanding behavior from single analytical approaches can be compared to the task of seeking linguistic insights by a chemical analysis of a book! Nevertheless, reductionist explorations at many levels, seeking a convergence of conclusions from different types of data, are essential before reasonable integration is possible. We may hope that an evolutionary perspective will be helpful in avoiding blind alleys or false leads in each type of study.

EVOLUTIONARY DEVELOPMENT OF THE BIOLOGICAL SUBSTRATE

Anatomical features have been inferred from extensive fossil records of man and other species. Little biochemical information can be generated from these sources. However, biochemical analyses of proteins of contemporary species seem to be consistent with the broad conclusions of the paleontologists.

Advances in protein biochemistry have permitted the determination of amino acid sequences of many homologous proteins and have justified the prediction that the amino acid sequence governs the conformational folding and biological activity of the protein (13). By comparison of such sequences, it is possible to infer some of the evolutionary events at the genetic level of nucleotide sequences in the DNA (14-16). We must stress at the start that the time scale of the evolution of proteins is in the millions of years, analogous to the time scale of the paleontologist. Two quite different and complementary approaches may be taken to the evolution of macromolecules: the first and better described is the highly conservative evolution of specific proteins, based upon nucleotide substitutions in the structural genes and amino acid substitutions in the protein; the second, more important for subsequent discussion of major departures in evolutionary development of species, points to more drastic effects of gene and chromosomal duplication that might permit saltatory consequences and development of altogether new functions.

The evolutionary origin of the relationship between the DNA code of triplets utilizing only 4 nucleotide bases (adenine, thymine; guanine, cytosine) and the 20 amino acids of common proteins is still unclear. Simulations of "primeval" atmospheric conditions have demonstrated that amino acids, purines, and pyrimidines can be generated from ammonia, hydrocyanic acid, methane, and carbon dioxide under ultraviolet and cosmic radiation (17). Hydrogen-bonded dimers readily form between adenine and uracil and between guanine and cytosine derivatives, without any requirement for enzymatic assistance. This inherent complementarity between purine and pyrimidine base pairs underlies the double-stranded helical structure of DNA. Mutation-induced single-base substitutions in the triplets sometimes cause no change in the amino acid specified (due to degeneracy in the code); otherwise they usually lead to replacement of one amino acid by another with fairly similar physical and chemical properties (18), producing a variant protein. More drastic amino acid replacements often require two of the three bases in the DNA triplet to be replaced. Thus, the DNA code is highly conservative in its effects on protein structure, indicating either that the code arose after proteins were formed or that the structures of the two kinds of macromolecules converged. The DNA, of course, is arranged in chromosomes in cells.

Two very complicated processes, subject to all sorts of metabolic, hormonal, and physical regulation and to exquisite timing during development, are required to produce proteins from the genes. The first, called transcription, is the formation of complementary RNA messenger from the DNA sequence in specifically-activated genes in a given tissue. (In higher organisms, hunks of RNA larger than the actual messenger appear to be made first.) The messenger RNA then combines with an RNA-protein complex (the ribosome) to form the protein synthetic apparatus upon which amino acids transported specifically by transfer RNA molecules can be linked together into the polypeptide structure of proteins. This second process is termed translation of the genetic message into protein effectors. The transfer RNA molecules are specific for each amino acid, but have many crucial characteristics in common, including their tiny size of about 80 nucleotides (10). They are surely ancient evolutionary components of the life process.

EVOLUTION OF ALLELIC GENE PRODUCTS

Changes in the DNA sequence occur spontaneously or upon induction by certain mutagenic agents. These changes are more or less random (depending upon the agent and the DNA and chromosomal structure). However, the nature of replication of the DNA and subsequent transcription and translation ensures that such a chance event will be perpetuated in the structure of the DNA and of the protein, with possible consequences in the function of the protein. The conservative nature of the relationship between the code and amino acids alluded to above reduces the risk that these chance events will be damaging to the organism. In addition, natural selection acts to eliminate sufficiently deleterious changes in proteins essential for survival. On the other hand, some changes may not affect protein function too severely or, rarely, may even improve the efficiency of the protein function in the usual environment or provide the adaptability to allow the organism to explore new environments. In this case, natural selection in favor of individuals carrying the new gene and protein combination may lead to accumulation of that new gene in the population. If the amino acid substitution is truly neutral in the functional and biosynthetic sense, its accumulation to a frequency above the low rate of such mutation must reflect the probabilistic processes of random genetic drift and effective population size.

When individual proteins, such as hemoglobins or cytochromes c, are compared among many species, sufficient homology of amino acid sequence is noted to "line up" the sequences and determine which sites remained unchanged during evolution, which sites allowed only some substitutions of similar amino acids, and which sites seemed to allow multiple or drastic substitutions while maintaining the overall function of these proteins (20-21). The number of amino acid differences (minimized by allowing gaps in the matching for maximum homology) as a function of the paleontological time scale can be used to estimate the rate of mutation – for several proteins listed in Table 3, roughly one effective (surviving) mutation per 100 amino acid residues per 1-10 million years. Rates may differ for different proteins or different species, and selection may markedly alter the effects for a specific protein; nevertheless, these allelic changes in genes for proteins which maintain their basic enzymatic or other activity can have little influence over the time scale of the evolution of man. The histones, basic proteins which combine with the DNA in chromosomes, are the most sluggish of all evolving proteins; comparable histones differ by only 2 amino acids (out of 101 residues) between the pea and the calf thymus (22). It will be interesting to learn how homologous are such distinctive nervous system proteins as the S100 and 14-3-2 proteins found mostly in glial and in neuronal cell populations, respectively, but each immunochemically indistinguishable over many species (23).

The slow evolution of homologous proteins with similar enzyme activity has incorporated at least one major development of complexity, however. Several examples, including the comparison of myoglobin and hemoglobin, point to the evolutionary development of allosterism of proteins (24). Allosterism refers to a thermodynamically-stabilized capacity of a protein to alter its conformation and thereby its activity upon interaction with inducers, cofactors, ions, hormones and inhibitors. The result is a regulation of protein function closely tied to physiological conditions of the tissue and to developmental needs. The implications of such capacities of proteins in the nervous system, for cell-cell interaction, for post-synaptic responsiveness to neurotransmitters, for learning consolidation, and for other complicated behavioral processes are apparent, though still speculative.

EVOLUTION BY GENE DUPLICATION

Major departures in evolutionary history must have required more drastic changes in the genome and in gene products than the amino acid substitutions we have been discussing. As Simpson has emphasized (1953), there is no basis for the notion of orthogenesis that evolution "progresses" steadily toward more complex or "higher" forms. Instead, features may become static, as the brain volume may have become in man, or regress, as olfactory structures clearly have. But how do new structures or new functions arise?

In a superb little book, Ohno (25) has pulled together notions of the effects of gene duplications dating at least from Haldane (26) and recent work of his own on evolution of vertebrate genomes, chromosome complements, and isoenzymes. Many striking chromosome changes in number are, in fact, highly conservative genetically, involving Robertsonian fusions and pericentric inversions. However, semi-sterility barriers introduced by inversions have undoubtedly been important in speciation, probably more so than behavioral or geographic isolation. Tandem duplication of cistrons by unequal crossing over at mitosis or meiosis within chromosomes has produced several significant features: 1) Capacity for producing multiple copies of the gene product, particularly ribosomal RNA and possibly ribosomal proteins and transfer RNAs. The most interesting evolutionary question here is the maintenance of functional, nearly identical yet redundant cistrons in the absence of apparent selective control. One explanation, which may be important for some CNS processes as well, is Callan's (27) master-slave model, in which only the master gene serves as the template for DNA replication after each cell division. 2) If the heterozygous state is advantageous, as for sickle hemoglobin, the incorporation of both alleles in a permanent form in the genome can be accomplished by having two loci. Otherwise, only a maximum of 50% of individuals can become heterozygous. Examples exist in the catostomid fish, whose esterase comprises a pair of variants, one active at 5° and the other variant at 20°C, the range of temperatures through which the fish must survive (28). A problem of gene dosage can occur, in that twice the usual number of enzyme molecules may be formed, especially if a pathway of related enzyme functions is involved. 3) Another response to the gene dosage problem is the differential regulation of former alleles, now duplicated loci, in different tissues as tissue-specific isoenzymes. Lactate dehydrogenase and fructose-diphosphate aldolase of the glycolytic pathway are examples of enzymes whose tissue-specific forms seemed to be well suited to the physiological needs of muscle and heart, as extremes for LDH (29), and muscle and liver, as extremes for aldolase (30). The highly duplicated immunoglobulin system also reflects this solution to gene dosage compensation: each plasma cell makes only one type of light and one type of heavy chain molecules. 4) Finally, we come to the major impact of gene duplication: the creation of a new gene product from a redundant duplicate of an old gene. As a redundant copy, the duplicate may absorb "forbidden" mutations that otherwise would have been eliminated by the conservative forces of natural selection, eliminated because of deficiency of the function of the old gene product. Once forbidden mutations begin to accumulate, there is the potential over long periods of evolutionary time for the appearance of useful new functions upon which natural selection will act favorably. Several instructive examples can be cited: (a) the pancreatic proteolytic enzymes trypsin and chymotrypsin (31); (b) myoglobin and the hemoglobins (32,33); (c) the light and heavy chains of immunoglobins (34); and (d) actin, the smaller of the muscle proteins that together make acto-myosin complexes, and the microtubule proteins of mitotic spindles, epithelial cilia, sperm tails, muscle sarcotubules, and axonal neurotubules (35). The microtubular proteins bind colchicine and guanosine triphosphate, while actin retains the capacity of binding a nucleotide, ATP. Little is known yet of the amino acid sequence homologies and detailed functional comparisons of microtubular proteins, particularly in the nervous system. Recent evidence suggests that brain microtubular proteins have a half-life of only 4 days and contain non-identical subunits of about

60,000 molecular weight (36,37).

Even though the amount of DNA and the number of chromosomes appear similar among the modern primates (38), an outstanding example of very recent duplication is the haptoglobin locus (39,40). This hemoglobin-binding plasma protein is highly polymorphic in all human populations, yet most non-human primates seem to have no variation in this protein. Probably a partial duplication occurred subsequent to separation of pongid and hominid lines. It is possible that similar processes of duplication and of unrestricted evolution of redundant sequences occurred in the enlarging forebrain and that the resulting macromolecular products are involved in learning and memory storage and in language functions.

REDUCTIONISTIC DESCRIPTION OF THE HUMAN NERVOUS SYSTEM

1. Anatomical Level

Several features have been identified as critical in the evolutionary development of the brain of man (Tables 4,5) (41,42). The grossest change is an absolute increase in the volume of the brain, from 400-550 cc in bipedal Australopithecus 2 million years ago to double that size 600,000 years ago in ancestors skilled with stone tools, to about 1300 cc in present day man. The volume of brain varies considerably among individuals, of course, and some estimates are based upon single or only a few fossil skulls (43). Fossil and contemporary brain sizes of ungulates and carnivores indicate that the trend to larger mean brain size is accompanied by an increase in the variance, as though diversity were greatly favored (44).

Underlying the rapid development in man of hand skills and social and linguistic skills is a striking relative enhancement in size and complexity of both the forebrain and the cerebellum. Meanwhile, olfactory structures have regressed and other structures have presumably been left a more subservient role. The pioneering histologist Ramon y Cajal established that neurons are contiguous, not continuous, at synapses and that the neurons are the metabolic, structural, and physiological units of the nervous system. Evolutionary increase in cell number leads to a geometric increase in potential axo-dendritic connections. New fluorescent histochemical methods that outline fiber pathways of specific neurotransmitter agents (45) offer powerful approaches to comparative studies of the connections between regions of the brain. In the morphogenesis of neural structures in man, two special features should be mentioned: 1) the fetal ganglionic eminence (46), a concentration of dividing cells, which go to form the basal ganglia and probably forebrain structures; analogous structures beneath the lateral ventricles have not been recognized in other species; and 2) a much longer time for maturation of the central nervous system in man. Unlike newborn apes and monkeys, who must be able to cling to their mothers, human newborns are delivered at a far less advanced stage of development, partly in evolutionary response to the narrowing of the bony birth-canal that accompanied bipedal locomotion. Presumably, such slow maturation is highly suited to molding of species-specific behaviors by cultural factors.

2. Neurophysiological Level

Many neuronal circuits appear to be genetically and developmentally "wired in" to function quasi-autonomously in the breathing and sucking of the newborn, in the precise regulation of temperature, pH and osmotic pressure of the internal milieu, in sleep, and in other essential processes. These functions are primarily mediated in the brain stem, diencephalon, and limbic system, while greater plasticity is assumed to be a characteristic of cortical functions (47). In the cortex, probabilistic spatio-temporal configurations have been invoked to describe firing patterns and a capacity for "relearning" complex functions after ablation of specific areas. We may expect that the psychological correlates of cortical function will have a greater variety and greater variability of neurophysiological and biochemical properties than will the brain stem and limbic structures whose functions were well established much earlier in evolutionary time. Computer-averaged evoked cortical potentials (48) and pharmacologically-manipulated electroencephalography (49) may be potentially useful descriptive and comparative techniques.

3. Biochemical Level

Biochemical and neurophysiological studies have demonstrated that the old view of a stable set of quiescent neurons that could be stimulated to action must be revised. The brain constitutes 2-3% of body weight, yet consumes up to 50% of the resting energy and oxygen supply. The "resting" state of neurons is characterized electrophysiologically by intense rhythmic and spontaneous activity. Likewise, protein biosynthesis and transport of proteins, structural components, and other molecules through the axon of the neuron are continuous, active processes. Fertile areas for comparative neurochemistry include the following:

a) DNA transcription

The result of differentiation of tissues is a selection of certain genes to be active in certain tissues, other genes to be active in other tissues, and some genes to be active in all tissues. DNA-DNA hybridization confirms that all cells contain the same DNA, while DNA-RNA hybridization confirms that only part of the genome is active in any tissue at any time (50). Some genes are redundant, coding for large amounts of ribosomal RNA needed for protein synthetic machinery. Appropriate methods can determine the proportion of "unique sequence DNA", genes present in single copies, that is transcribed into RNA messengers. In most tissues, only 3-6% of this DNA is transcribed (51,52). In brain tissue, a remarkably higher proportion is transcribed— 10-13% in the mouse and 20% in man (52). McCarthy and his colleagues are now testing different regions of the brain to see whether cortical regions utilize even more of the genetic complement than do brain stem or other regions. It will be interesting to determine whether stimulation by learning tasks or electrical means can increase the transcription activity even further. The theoretical limit is 50%, since only one or the other of the two DNA strands is transcribed along any portion of the double helix. Of course, it is not at all clear yet what the "extra" DNA is used for in brain, possibly to provide a complex variety of RNA or protein for recognition, integration, and memory-storage functions.

b) Compartmentalization of protein synthesis

Neurons appear to be more highly compartmentalized than other tissues in their capacity for protein synthesis and in its coupling to specialized neuronal functions (53). Whether there are differences between regions of the brain or between man and other species is not clear. In large neurons, the cytoplasmic ribosomes are concentrated near the endoplasmic reticulum of the Nissl substance in the perinuclear region, the initial segment, and the axon hillock (54). A high proportion of these ribosomes are not attached to the membrane of the endoplasmic reticulum and may function directly in the synthesis of protein involved in axoplasmic transport to the nerve ending. Brain ribosomes require a high concentration of potassium ion (100 mM), suggesting a link with bioelectric phenomena and active transport of K^+. Brain mitochondria have their own apparatus for active protein synthesis, do not require an external source of ATP, are inhibited by the antibiotic chloramphenicol and not by ribonuclease. Mitochondrial protein synthesis is tightly linked to oxidative phosphorylation, increasing under conditions optimal for the latter and being inhibited when specific inhibitors of oxidative phosphorylation like rotenone and antimycin A are present. Finally, nerve ending fractions called synaptosomes carry on protein synthesis, with synergistic stimulation by appropriate concentrations of Na^+ and K^+. The ionic concentrations required for maximal incorporation of amino acids into protein also result in maximal sodium-potassium ATPase activity, K^+ uptake, and oxygen uptake. Ouabain, which inhibits the Na-K ATPase activity, markedly inhibits synaptosomal protein synthesis, further suggesting a close coupling of the synthetic activity with the ionic flux and energy metabolism in the nerve ending.

c) Specificity and Variety of Neurotransmitter Agents

Synaptic inputs can be either excitatory or inhibitory, and neurotransmitter function has been attributed to an increasing array of chemical agents. The evidence is good for acetylcholine, norepinephrine, dopamine, serotonin, and gamma amino-butyric acid that such agents are concentrated in synaptic vesicles, can be isolated and specifically taken up against a concentration gradient in vitro into isolated synaptosomes, and are probably released upon physiological stimulation across the synaptic cleft to excite (depolarize) or inhibit (hyperpolarize) post-synaptic membranes. The post-synaptic membrane has specific receptors for the action of these agents. Nevertheless, only a minority of all synapses can be assigned to even these incompletely proved transmitter agents; it is likely that a variety of amino acids (histamine, glutamate, aspartate, glycine) and possibly other compounds act as transmitters in certain fiber pathways (55). The potential for evolutionary diversity and functional specificity is great.

d) Membranes and Potential Macromolecules for Recognition Processes

The formation of cell-cell contacts, the specific migration of neuronal cell groups, and the processes of selective cell death may be mediated by macromolecules incorporated into the membrane structure of nerve cells. Complex glycoproteins are among the potential mediators (56). Much of the work on this subject is still at the level of model systems, but rapid technical advances offer promise of substantive progress. We should emphasize that the diversity of specific proteins has been derived from a "simple" triplet code based upon only 4 different nucleotide base "letters". Thus, it is not unreasonable to expect sets of macromolecules to be able to perform complex memory storage and cell recognition functions, for the variety of intra-membrane geometric arrays that could be formed with, for example, 10 different protein or carbohydrate-protein units in different combinations is enormous. It will be important in comparative biochemical studies to determine whether human cortical neurons have a greater variety of such units than other species.

Discussion of complex molecular functions centers on the role of proteins, as will our discussion of the evidence for molecular evolution. Proteins have been termed "universal biological effector molecules" (57), for they act as enzymes for metabolic processes, as components of structural neurotubules and membranes, as recognition molecules for the neurotransmitters released across synapses, and possibly as electrogenic effectors for ion gating changes in the propagation of action waves down the axonal membranes. Monod (24) has emphasized the capacity of proteins to act as molecular agents of structural and functional teleonomy - mediating oriented, constructive, and coherent activity through their ability to "sense" substrate or inhibitor concentrations, to carry in their structure the information for proper conformational folding as a response to such inputs, and to catalyze metabolic reactions or macromolecular interactions.

Although a biochemical basis for the characteristic human functions of cognition, language, and consciousness is beyond description at present, modern techniques of human genetics do allow us to demonstrate the individuality and uniqueness of different humans at a biochemical level and provide a basis to speculate about evolutionary mechanisms that must underlie the biological substrate of behavior.

PROTEIN POLYMORPHISMS

The ability to detect small differences in the structure of proteins, which reflect qualitative differences in the respective genes, permits an experimental approach to the question of human individuality. The basic technique involves electrophoresis of tissue extracts and specific staining for enzyme activity. Since electrophoretic mobility is based upon net charge of the protein and may be altered by an amino acid substitution that changes net charge (about 30% of single-base substitutions), specific enzymes or other proteins can be compared in many individuals from a given species. Rare, variant proteins are found in single individuals, simply on the basis of continuing mutations. However, common variants (arbitrarily defined as 1% gene frequency) require some selective advantage or random genetic drift in order to have accumulated and are of great interest as "polymorphisms" both for questions of their origin and for application to the description of individuals. Using ABO and other red blood cell antigens, serum proteins, certain serum and red blood cell enzymes (Table 6) plus the histocompatibility antigens, Lp antigen, and new red cell enzymes as testable polymorphic systems, the likelihood of finding two humans with identical results (except for monozygotic twins) is on the order of 1 chance in 3 billion (about the size of the world's population). And only a small fraction (much less than 1%) of the estimated number of protein polymorphisms has been discovered (Table 7).

Selective forces have been identified for the remarkable polymorphisms of sickle hemoglobin (up to 40% of individuals are heterozygous in parts of Africa) and glucose-6-phosphate dehydrogenase deficiency. Resistance of the heterozygote to early death from malarial infection seems to provide a definite example of natural selection in man (11,12). For all the other human polymorphisms, we do not know whether their presence represents the effect of past or current selective forces or is due to random genetic drift. Recent data of clines of gene frequencies (58) and models for gene disequilibrium and selection for whole regions of chromosomes (analogous to the genes locked into chromosomal inversions in Drosophila) (9) make it plausible that many more polymorphisms are maintained by selection without introducing too severe a genetic load. However, many polymorphisms such as phosphatases, esterases, and peptidases, represent in vitro activities of enzymes which cannot be assigned specific metabolic reactions in vivo.

CURRENT STUDIES OF ENZYME VARIATION IN HUMAN BRAIN

We have recently embarked upon a novel application of biochemical genetic techniques and the notion of enzyme polymorphisms in the central nervous system of man. The rationale is as follows: Enzyme surveys in Drosophila, mice, and man indicate that about 30% of enzymes have common variants that can be detected by the electrophoretic screening method. Most of these electrophoretic variants that have been studied have a significant difference in quantitative enzyme activity, compared with the usual form of the enzyme (Table 8) (59). For example, G6PD A+ has 85% and G6PD A- 15% of the activity of the usual G6PD B form; and the three alleles of acid phosphatase, occurring in dimers, have relative activities of 100, 150 and 200. The acid phosphatase model is of special importance, for a quantitative survey in human populations suggests a normal distribution of enzyme activity; only with electrophoretic differentiation of the 6 dimeric phenotypes (AA, AB, AC, BB, BC, CC) can each subgroup be tested and be shown to have narrow ranges of enzyme activity (Figure 1) (60). Unfortunately, the in vivo role of this interesting enzyme has not been elucidated.

We have selected crucial metabolic pathways and examined the relevant enzymes for the possibility of variant forms of the enzymes (61). A polymorphism of a rate-limiting enzyme, such as phosphofructokinase in the pathway of glycolysis (Figure 2), would be highly significant even if associated with only a small difference in quantitative enzyme activity, since production of lactate at the end of the pathway and of ATP along the way would be affected. On the other hand, a small difference in activity of an enzyme normally present in concentrations well above rate-limiting activities could be expected to have no such consequences. Thus far, our attention has been directed primarily to the energy-generating metabolic processes of the nervous system. The brain is exquisitively sensitive to lack of oxygen or glucose, irreversible damage occurring within 5 minutes in man. The prime metabolic pathway for glucose utilization is glycolysis. We have screened all 11 enzymes of this pathway from hexikinase to LDH in some 135 human brain specimens. None of these enzymes has a common variant form. Only single, rare variants of phosphoglycerate kinase and of enolase were found (Table 9), presumably reflecting mutation. This negative finding may be highly significant (62) since similar lack of frequent variation was noted in our screening of mouse and monkey brain (63) and in screening of human erythrocyte enzymes of the glycolytic pathway by Chen and Giblett (64). The only exceptions are the well-established polymorphisms in other tissues of PHI in the mouse and of PGK in certain human populations (New Guinea).

These two enzymes are present in high activity relative to other enzymes in the pathway. It is possible that the very old evolutionary status of glycolysis and its central role as the primary pathway of glucose utilization in the brain have placed remarkable constraints on the tolerance for mutation-induced variation in the protein structure of these enzymes. Most of the glycolytic enzymes have evolved tissue-specific isoenzyme forms — that is, different genes specify proteins with similar enzyme function in different tissues (e.g. brain versus muscle). There are clinical consequences of such tissue variation within individuals. If an enzyme is deficient in erythrocytes, one would expect deficiency in other tissues only if the same gene specified that enzyme in the other tissues. Deficiencies of seven of the glycolytic enzymes have been identified as causes of hereditary hemolytic anemia in man. From their electrophoretic and biochemical properties, only 3 (PHI, TPI, PGK) are likely to have the same form in brain as in red blood cells (65). The original case reports of TPI and PGK deficiency did note prominent nervous system symptoms and signs. The PHI deficiency is not instructive, since the deficiency was mild even in the red blood cells. Deficiency of the other enzymes was not associated with any neurologic abnormalities. Such tissue comparisons are important for another reason: if the same gene is responsible for the enzyme in all tissues, sampling of blood or skin or hair follicles may enable us to test for properties of the brain enzyme without needing to obtain brain tissue.

Another aspect of the conservatism of the glycolytic pathway is a comparison with the pentose-phosphate shunt. Here the first two enzymes have been studied, G6PD and 6PGD. These enzymes are controlled by the same gene in the nervous system as in other tissues and the same polymorphism known to exist in RBCs occurred in our brain specimens. We hope to extend study of this auxiliary enzyme pathway to additional enzymes to test the prediction that polymorphism is more likely in the less essential pathway.

A new polymorphism in man has been uncovered in our screening of the brain material (66). Malic enzyme, NADP-linked malate dehydrogenase, exists in a cytoplasmic form which probably inter-connects the Krebs cycle and gluconeogenesis and in a mitochondrial form, whose function is speculative, but may be involved in particulate hydroxylation reactions. Studies in man and in monkeys demonstrate that the cytoplasmic and mitochondrial malic enzymes are controlled by different genes and vary and segregate independently. The mitochondrial malic enzyme in man has 3 phenotypes in starch gel electrophoresis, corresponding to gene frequencies of 0.7 and 0.3 for the two alleles.

The generation of high-energy phosphates is mediated first from stores of creatine phosphate in the nervous system. A striking variation in the activity of CPK with absent, intermediate, and intense activity in different specimens is suggestive of a difference in stability or kinetic parameters of a possible variant. Characterization of these findings is in progress.

Other enzymes studied thus far include glycerol-3-phosphate dehydrogenase, rate-limiting for myelination; isocitric dehydrogenase, an NADPH-generating enzyme which has disproportionately high activity in premature infants, as compared to full-term infants or older individuals; and glutamic dehydrogenase and acetyl cholinesterase, enzymes involved in pathways affecting the neurotransmitters gamma amino-butyric acid and acetyl choline, respectively.

We intend to expand the study to other enzymes, particularly those involved in nerurotransmitter metabolism and biosynthesis, with the expectation that biochemical correlates of neural plasticity may more likely be found in such pathways than in the basic energy-generating processes, like glycolysis. In addition, study of monoamine oxidase, glutamic acid decarboxylase, and other such enzymes allows the marshalling of a second powerfül experimental tool of the biochemical geneticist: pharmacogenetic analysis. When certain drugs are given to a large number of people, the therapeutic response or incidence of side effects has a strikingly bimodal distribution, suggesting a major difference in the two groups of individuals. In several cases the biochemical mechanisms underlying such differences have been demonstrated. For example, about half of the Caucasian population acetylate such drugs as isoniazid, hydralazine, dapsone, and sulfas rapidly, while the other half of the population acetylate slowly. The rate of acetylation in the liver is determined by a single recessive gene (slow is recessive). Slow inactivators reach higher blood levels of active drug and higher risk of toxicity. Many of the brain enzymes of interest have known specific inhibitors, with which it will be possible to screen many individuals for variants in susceptibility to inhibition by such drugs. Since these drugs have definite pharmacological and behavioral effects in vivo, such a genetic difference in response to these agents would allow direct manipulation of the appropriate neurotransmitter pathway (in mouse or monkey models and, with careful ethical controls, in patients receiving such drugs for therapeutic indications). The observations that a variety of psychopharmacologic agents can modify affect, sleep, cognition, and sensory perception constitute a cornerstone of our assumption that such functions of the MIND are mediated by the metabolic processes of the BRAIN (67). It is likely that we have only uncovered the tip of an iceberg of specific enzyme-drug interactions that underlie the marked differences between individuals in their response to drugs and in their risk of side effects.

Study of polymorphic enzyme systems involving crucial metabolic processes in the brain seems a potentially fruitful approach to polygenic phenomena that underlie most behavioral traits. The electrophoretic screening method is capable of uncovering qualitative, structural differences in specific enzymes between individuals, without confusion by the alteration in quantitative activity in different parts of the brain or upon physiological stimuli. However, the interpretation of the physiological consequences of these qualitative enzyme differences will require careful measurement of the metabolic impact in individuals having the two different types of enzyme. In humans such measurements must be carried out indirectly with radioactive tracers and with enzyme inhibitors; in model systems in mice or monkeys more direct measurements may be feasible. The statistical notion that polygenic inheritance involves the equal and additive effects of a great many genes must be modified in light of metabolic interactions. Certain metabolic control points will be more important than others and much more important than enzyme reactions in minor pathways. Thus, it is possible that, even though a great many genes can interfere with normal brain development if completely deficient, the so-called normal range of development and function may be determined by a relatively few polymorphic genes sitting at rate-limiting steps in key metabolic pathways. Since we have already ruled out such a polymorphism for glycolysis, it is likely that the rate-limiting points in the metabolic scheme of the brain that do have variation will be fewer than the potential number of sites. The fact that a normal or Gaussian distribution of some quantitative variable is obtained does not require a large number of genes for explanation. In fact, with just two alleles at each of two interacting loci or with three alleles at a single locus (acid phosphatase model), a quantitative distribution of some resulting trait can appear polygenic (59). The key feature of this model for congenital malformations or for classification of development as normal versus abnormal is the presence of a threshold in the quantitative sense, a threshold to which each allele can contribute and upon which various hormonal and environmental agents might act. The heuristic value of this point of discussion is to encourage the search for major gene mechanisms in polygenic traits and psychiatric disorders.

APPROACHES TO COMPLEX BEHAVIORAL PHENOTYPES

It is difficult to analyze phenotypes into meaningful "units" of behavior, in the sense that molecular evolution can be analyzed in the units of proteins, DNA, and chromosomal structures or that the underlying biochemistry for the brain might be analyzed in terms of energy requirements, developmental switches, recognition phenomena, and possible electrochemical transformations. However, we have identified five operational approaches that may signify possible "handles" on certain aspects of modifiable behaviors at the level of integrated functions of the nervous system.

1. Sexually dimorphic behavior and the effect of fetal and neonatal hormones.

One of the more difficult and especially timely questions about human behavior is the issue of male/female differences and the extent to which they reflect cultural impact of the assigned sex role or biological impact of the sex chromosomes and sex hormones. Goy, Phoenix, Young and their co-workers (68,69) have studied in the guinea pig, the rat, and the rhesus monkey the organizing or sex-differentiating action of fetal gonadal substances on behaviors beyond that which is primarily sexual. It was long ago established that mammalian fetuses lacking or deprived of fetal testes would undergo "indifferent" embryological development to normal female form and psychosexual orientation. Fetal testicular hormone is essential for differentiation of the Wolffian duct system into the male genital tract and for suppression of the Mullerian duct system. With female guinea pigs, prenatal injection of androgen produced a marked display of masculine behavior, as well as a lowered capacity to display feminine behavior (up to 92% later failed to come into heat) (68). Conversely, castration of genotypic male rats led to significant postpubertal display of feminine behavior, measured as lordotic receptivity in response to mounting by intact males. Injection of testosterone propionate to the pregnant mother rhesus monkey caused genetic female offspring to later display behaviors distinctly shifted in frequency toward the male values. The measured behaviors are patterns of threatening, play initiation, rough-and-tumble play, chasing play, and immature double-foot-clasp mounting. In all cases, the differences between males and females are quantitative, not qualitative. The clinical implications of such studies for disorders of psychosexual identity in man are obvious. Money (70) has found that hermaphroditic individuals raised in one sex, matched by individual of identical diagnosis raised in the other sex, typically differentiate psychosexually in concordance with the parentally assigned sex. However, male transsexuals, some homosexuals, and occasional Klinefelter's syndrome patients with the XXY chromosomal anomaly tend to develop a gender identity resembling normal female, rather than normal male patterns (71). The distribution of these behaviors is shifted in males versus females, though a good deal of overlap exists.

The physiological bases for sex-specific patterns of behavior are uncertain, but certain hypothalamic regions are known to be excited or inhibited by the sex hormones, regions that might be involved in neural motivational systems. The potential for molecular biological exploration of such hormone-sensitive regions is at hand. For example, stereotactic implants of estradiol in the diencephalon of the female rat distinguish two hypothalamic centers sensitive to estrogen: destruction of the gonadotropin-regulating center in the anterior hypothalamus, or implantation of estrogen there, leads to gonadal atrophy; lesions in the basal tuberal-median eminence suppress mating behavior, but do not affect the gonads or interfere with the estrus cycle in the rat or cat (72). Estrogen-sensitive oviduct and uterine preparations contain estrogen-binding cytoplasmic and nuclear proteins (73). Similar binding sites probably exist in the sensitive regions of the hypothalamus and possibly in higher brain centers. In the Mongolian gerbil, implantation of minute amounts of testosterone in the pre-optic region of the hypothalamus of castrated males can restore the species-specific and male-specific behavior of territorial marking and such effects of testosterone can be blocked by simultaneous implantation of reasonable amounts of Actinomycin D or puromycin (74).

Testicular feminization, a syndrome in which genetic males with normal testes and normal production of testosterone fail to become masculinized because the target tissues fail to respond to the hormone, is now being studied in an animal model (75). These individuals appear and act as females. In the various studies in animals and in man, it may be possible to determine central nervous system mechanisms of sexually dimorphic behaviors.

2. Inborn Errors of Metabolism in Man

A striking array of enzyme deficiencies has been recognized as "experiments of Nature" in man. Some of these are associated with mental retardation or other behavioral abnormalities, others affect only red blood cells or other tissues, and some seem to have no detectable deleterious effects. Most are inherited as autosomal recessive traits, though a few are X-linked recessive traits manifested in males in hemizygous form. We have recently tabulated a variety of amino acidurias, carbohydrate and lipid and mucopolysaccharide storage diseases, and miscellaneous metabolic errors according to their impact on the nervous system (65). A few of these syndromes are listed in Table 11. We distinguished a gross defect in mental development from more specific neurologic signs or psychiatric/ psychological disorders, occurring without mental retardation or before mental deterioration. Some of these disorders are due to toxic effects of metabolites accumulated as a result of metabolic defects in other tissues, while other disorders are intrinsic to the nervous system. Among the latter, two of great interest are the Lesch-Nyhan syndrome and homocystinuria. The Lesch-Nyhan syndrome comprises hyperuricemia, choreoathetotic movement disorder, and a self-destructive, impulsive behavior. It is due to deficiency of an enzyme known as hypoxanthine-guanine phosphoribosyl transferase (HGPRT), involved in what was previously discounted as a minor "salvage" pathway of purine metabolism. This enzyme turns out to have its highest activity in the body in the basal ganglia of the brain, allowing a correlation with the neurologic disorder of choreothetosis. Just how to relate this metabolic disorder to the impulse to bite off the phalangeal tips of the fingers or the lips or to poke one's own eyes uncontrollably is a clear challenge, thus far lacking a response. The importance of the metabolic pathway is underscored by the finding that heterozygous females (cellular mosaics by the process of random X-inactivation for this X-linked trait) have the expected 50% of normal activity for HGPRT in skin fibroblasts, but 100% of normal activity in blood cells (76). Presumably, all blood cell precursors lacking HGPRT activity were eliminated. We have no information on HGPRT-negative cells in their nervous system.

A second remarkable metabolic error intrinsic to the nervous system, as well as other tissues, is homocystinuria, due to deficiency of the enzyme cystathionine synthetase. As a result, cystathionine is not formed and homocystine and methionine accumulate. Cystathionine is a complex amino acid found normally in remarkably high concentrations in the brain, but its function is entirely unknown. A different inborn error, cystathioninuria, due to deficiency of the enzyme to break down ystathionine, seems to be unassociated with any major defects. Clinically, homocystinuria is characterized by vascular thromboses, skeletal anomalies, downward displacement of the ectopic lens of the eye, and — in only about one-half of cases — mild to moderate mental retardation. There is considerable dispute whether affected patients or their sibs might have an increased incidence of schizophrenia; the evidence is not impressive, but the question was a sound speculation, based upon the hypothesis that methylated derivatives of normal neurotransmitter substances might be pathogenetically involved in schizophrenia...or at least in simulating hallucinatory states. Why only one-half of cases have mental retardation is unclear. Perhaps the others have lower IQ than would have been their potential, but still within the "normal range". Perhaps the enzyme defect is different in different individuals.

A most important consideration in these rare recessive inherited metabolic disorders is the realization that even a disease with an incidence of only 1 in 40,000 births is associated with a heterozygous carrier frequency of 1%. For certain enzymes present in the brain and present in near rate-limiting activity, such a decrease to 50% of normal activity in the carrier might be a significant factor in predisposition to mild mental impairment or possibly to regionally specific mental defects. There has been very little detailed psychometric study of such possibilities. The only definite finding comes not from a metabolic error but from the chromosome anomaly 45,XO or Turner's syndrome, in which Money (77) has demonstrated a striking defect in space-form relationships and in drawing ability. Anderson, however, has initiated a series of studies of manual dexterity and related specific functions in patients and carriers of the gene for PKU (78,79). Since carriers for the long list of rare recessive diseases together make up a large percentage of normal individuals, any mild abnormalities that could be documented in such carriers might be useful in interpreting the range of normal behavior. Study of enzyme systems identified by syndromes of metabolic disorders seems complementary to our systematic approach, described earlier, to enzyme variation in the key metabolic pathways of the nervous system. A rational search for behavioral effects of another syndrome was reported by Scriver (80). Since the amino acid transport defect of cystinuria is present not just in kidney and intestine, but also in brain, it was reasonable to seek clinical consequences. The scattered cases of variable psychiatric disorder or mental retardation associated with cystinuria may not be a greater incidence than that due to chance, however.

For all such studies, more careful and more discriminating tests of psychological functions are needed. Some progress in this regard has been reflected in studies of brain-injured patients (81).

3. Inter-racial differences

The possibility of individual and racial differences in behavior before any obvious post-natal learning has been tested in a preliminary fashion (82). A matched series of infants (5-72 hours of life) of Chinese-American (Cantonese background) and of European-American background were evaluated on a Brazelton scale of 25 neurological and behavioral criteria. They were identical in scores of sensory and motor development, central nervous system maturity, and interest in their social environment. But there was a striking difference in scores of temperament, especially excitability/imperturbability ratings, such that the Chinese-American infants were less changeable, less perturbable, habituated more readily, and were consoled or calmed themselves more readily. The results are so consistent with a stereotype of adult behavior that further studies of this type will be of great interest.

There are definite differences in the gene frequencies for various polymorphic proteins in blood of oriental, negroid, and caucasoid populations (60,83). There may be similar inter-racial differences in gene frequencies for enzymes in the brain and other tissues. Physiological differences might result from such polymorphic protein systems, but the impact of cultural forces on the biological substrate makes evaluation of behavioral phenotypes for inter-racial differences a most difficult task.

4. Polymorphisms of EEG Phenotypes and Possible Behavioral Correlates

Vogel has summarized a monumental study of electroencephalographic (EEG) patterns in presumably normal individuals. The complex electrical potentials recorded from the scalp are determined almost finding comes not from a metabolic error but from the chromosome anomaly 45,XO or Turner's syndrome, in which Money (77) has demonstrated a striking defect in space-form relationships and in drawing ability. Anderson, however, has initiated a series of studies of manual dexterity and related specific functions in patients and carriers of the gene for PKU (78,79). Since carriers for the long list of rare recessive diseases together make up a large percentage of normal individuals, any mild abnormalities that could be documented in such carriers might be useful in interpreting the range of normal behavior. Study of enzyme systems identified by syndromes of metabolic disorders seems complementary to our systematic approach, described earlier, to enzyme variation in the key metabolic pathways of the nervous system. A rational search for behavioral effects of another syndrome was reported by Scriver (80). Since the amino acid transport defect of cystinuria is present not just in kidney and intestine, but also in brain, it was reasonable to seek clinical consequences. The scattered cases of variable psychiatric disorder or mental retardation associated with cystinuria may not be a greater incidence than that due to chance, however.

For all such studies, more careful and more discriminating tests of psychological functions are needed. Some progress in this regard has been reflected in studies of brain-injured patients (81).

3. Inter-racial differences

The possibility of individual and racial differences in behavior before any obvious post-natal learning has been tested in a preliminary fashion (82). A matched series of infants (5-72 hours of life) of Chinese-American (Cantonese background) and of European-American background were evaluated on a Brazelton scale of 25 neurological and behavioral criteria. They were identical in scores of sensory and motor development, central nervous system maturity, and interest in their social environment. But there was a striking difference in scores of temperament, especially excitability/imperturbability ratings, such that the Chinese-American infants were less changeable, less perturbable, habituated more readily, and were consoled or calmed themselves more readily. The results are so consistent with a stereotype of adult behavior that further studies of this type will be of great interest.

There are definite differences in the gene frequencies for various polymorphic proteins in blood of oriental, negroid, and caucasoid populations (60,83). There may be similar inter-racial differences in gene frequencies for enzymes in the brain and other tissues. Physiological differences might result from such polymorphic protein systems, but the impact of cultural forces on the biological substrate makes evaluation of behavioral phenotypes for inter-racial differences a most difficult task.

4. Polymorphisms of EEG Phenotypes and Possible Behavioral Correlates

Vogel has summarized a monumental study of electroencephalographic (EEG) patterns in presumably normal individuals. The complex electrical potentials recorded from the scalp are determined almost entirely by genetic factors. Monozygotic twins share not only identical EEG patterns, but identical maturational transitions in the EEG patterns in adolescence and in later life. Analysis of pedigrees (84) points to a polygenic mode of inheritance, with several specific variant EEG patterns inherited as Mendelian autosomal dominant traits.

Four percent of the population have the monotonous tall alpha pattern, determined by a single autosomal dominant, and another 5-10% have a beta wave pattern, with multifactorial determination. For both groups limited data suggest that individuals of either of these variant EEG types tend to marry individuals of the same EEG type (Table 12). And for another anomalous EEG pattern of less straightforward inheritance (posterior slow rhythm) there may be, as yet poorly characterized, predisposition to psychiatric disorders. Apparently, discriminating psychometric analyses of individuals with different classes of EEG patterns have yet to be carried out. Also there is the potential to correlate the EEG patterns and any psychometric features with response to physiological (photic, auditory, sleep) stimuli and to pharmacological stimuli and to learn whether individuals of a given EEG pattern have distinctively different susceptibility to various sedative or psychoactive drugs.

5. The Effects of Psychopharmacologic Agents

> "A desire to take medicine is, perhaps, the great
> feature which distinguishes man from other animals."
> Sir Wm. Osler, 1891

The potent effects of various drugs as sedatives, anesthetics, and central stimulants are well-established, though there is very little evidence on individual differences in susceptibility to desirable or toxic effects. Several classes of drugs have proved effective in treatment of affective disorders; here certain clinical studies suggest that groups of patients may differ in their responsiveness or lack of responsiveness to monoamine oxidase inhibitors or to tricyclic anti-depressants (85,86). Such patients manifested a similar pattern of response when treated during a subsequent episode of depression, as did relatives who were treated for depression. The bewildering array of "up" drugs used in all sorts of combinations by hippies and housewives alike impress the "street people" with the variety of response in different individuals. Always there is the suspicion that individuals who have "bad trips" may be predisposed to psychiatric difficulties. We have been reluctant to test L-DOPA or other possible provocative agents in patients with a risk to develop Huntington's chorea, for the similar reason that we might induce psychotic symptoms in a predisposed patient and be unable to reverse the process. Finally, we should mention the current interest in hyperactive or hyperkinetic children and the recommendations (87) that some 5-15% of young children be treated with amphetamines or methylphenidate (Ritalin). Here we are dealing with a potential culturally-decided behavioral modification program of generalized scale and frightening possible impact. The underlying behavior at issue is usually poorly characterized; the pharmacological basis for the treatment suspect; the biochemical actions of the drugs both uncertain and, in the case of Ritalin, beyond the reach of available analytical chemical techniques. Nevertheless, the widespread use of amphetamines in the adult population and the acceptance of tranquilization of neurotic as well as psychotic individuals provides a cultural background suited to increasing modification of behavior with psychoactive drugs. This issue seems deserving of attention and control. The neuro-behavioral scientist has much to offer in studying the individual differences in mechanisms of response to these drugs and in providing a rational basis for their use.

THE CENTRAL ROLE OF LANGUAGE IN THE EVOLUTION OF MAN

Essentially all writers agree that symbolic, verbal communication in the media of language is the hallmark of *Homo sapiens*. Complex coordinating, representational, and cognitive functions of the human central nervous system are identifiable in other species. Animals, of course, may have elegant means of communication, too, but we assume that they lack the capacity to create subjective experiences, to carry out "subjective simulation" (24), to appreciate the notions of death and of "self". Burial of the dead as an indication of such symbolic understanding appears in the fossil record very much later than the evidence of upright posture, apposed thumb, man-like jaw, and enlarged brain. However, *Homo neanderthalensis* had enough compassion to bury the dead and decorate the grave with flowers, presumably reflecting intellectual capacity greatly in excess of what was needed to cope with the environment of the time. The timing of origin of language is altogether uncertain, and most modern linguists seem to ignore the issue.

A remarkable transition has occurred in the field of linguistics in the past decade or so. Previously, attention seemed to be riveted on the diversity of language and the possibility of tracing languages in cultures through what are now regarded as superficial aspects of vocabulary and grammar. Swadesh and others derived "evolutionary trees" of language inter-relationships, analogous to the trees drawn by the paleontologist or the molecular taxonomist (Figure 3). This technique of estimating "time-depth" of language relationships, called glottochronology or lexicostatistics (88-90), assumed that spoken language could be divided into core and general word lists, that the rate of retention of vocabulary items in the core is constant through time and in all languages (about 80% retained over 1000 years). By a simple calculation, from the percentage of true cognates between any two languages, the length of time that has elapsed since the two languages began to diverge from a single parent language can be estimated. Thus, the evolution of language appears similar to the evolution of proteins, alterations in spelling or form of words being analogous to the amino acid substitutions in the proteins. Linguistic and blood group data, in fact, were used together by Watson et al. in an anthropological study in New Guinea, a large island where 2-3 million people are divided into some 400 language groups (91). The major difference between the paleontological or molecular evolutionary trees and the trees of the glottochronologist lies in the time scale — millions of years for the biologists versus hundreds of years for the glottochronologist. It is this difference in time scale that reflects the impact of cultural evolution.

Chomsky and other modern linguists have described a basic unity in the midst of the diverse languages of man (92). There is no explanation why any particular pattern of sounds signifies any given object or action (except onomatopoeia). Yet speech pattern of all languages operate on a few basic principles and the semantic patterns may well be reducible similarly if deep structures are deciphered. The analysis employs a universal phonetic alphabet and levels of grammaticality starting with phones and advancing through phonemes, morphemes, and lexemes. Such a unifying approach points to some biologically-determined potential of the species and sets a model for analysis of other features of man's culture.

As described by Lenneberg (93,94), language has its roots in the physiological processes of cognition. Language-knowledge is viewed as an activity, rather than as a static storehouse of information; an activity of extracting peculiar relationships from the environment and interrelating these relationships. Examples drawn from neurologic disorders show a parallel between acquired language disturbances and acquired disorders of such cognitive features as perceptual recognition. In the evolutionary context, it has been claimed that primates seem to have adequately developed motor systems for vocalization (95) and visual-auditory perceptiveness for such clues to relationships (96).

There is controversy about the possibility that the laryngeal and pharyngeal anatomy has evolved in parallel with the development of a capacity for language in the brain. Bryan (97) claims that, although isolated larynxes appear identical, anatomical relationships and function of the epiglottis and soft palate and insertion of the base of the tongue make babbling and a variety of vocalizations easy only in man. Lenneberg (94) agrees that structural changes in the vocal tract make the production of speech sounds uniquely possible in man, but insists that such modifications are not prerequisite for language capacity. Thus, children with deformed fauces can learn to understand English, even though their own speech is unintelligible. Also, children with congenital deafness, congenital blindness, or mesencephalic lesions that interfere with muscular coordination for speech can acquire language skills (93).

Attempts to teach chimpanzees some form of human language suggest that the vocal tract difference is of some importance. Chimps Viki (98) and Gua (99), despite long efforts, acquired only a few words of barely intelligible English ("mama", "papa", "cup", "up", for example). The Gardners (100), however, noted that this sociable animal which forms close relationships to humans tends to be silent and to vocalize only when excited. Instead, chimps use their hands extensively to communicate. On the hypothesis that gesturing by chimps might be a natural mode of expression, like bar-pressing for rats or key-pecking for pigeons or babbling for humans, they exposed Washoe to the American Sign Language gestures of the deaf and "taught" signs and rewarded learning. It is useful that some of the signs are iconic, while others are arbitrary. Washoe was an 8-14 month old female at the start of the program. Within 22 months of the project, she could use 30 signs. From the time she had 8 to 10 signs in her vocabulary, she began to string two or more together and to transfer spontaneously a single sign to a wide class of appropriate referrents. In these days of heroic organ transplantation, it would be interesting to transplant a human brain into a chimp and listen! Probably a good deal of input "talk" would be necessary, as well.

Among the great many inherited and developmental syndromes affecting man, none seems to specifically alter language. However, there is interest in the speech impairment that accompanies half of the cases of histidinemia and in the possibility of metabolic abnormalities in some cases of reading impairment (dyslexia) (101).

It probably is not appropriate to view language itself as the evolutionary advance in the development of man; rather, language reflects some saltatory developments in complexity of cognitive processes. Although ablation or infarction of certain frontal and temporal cortical areas leads to aphasic defects in speech, it is likely that no specific anatomical structures in the brain can be assigned language function. Perhaps we have not adequately tested for such functions, however. For example, it has been a surprise that such a vague, diffuse, and varied function as affective state or mood could be localized to the limbic system, that stimulation or lesions in limbic structures can cause tameness or aggressiveness, hypersexuality, change in feeding or drinking or emotional expression, or recent memory impairment (102). In the cerebral disconnection syndrome produced by complete section of the corpus callosum between the dominant and non-dominant hemispheres (103), disruption of inter-hemispheric integration produces remarkably little disturbance in ordinary daily behavior, temperament, or intellect. Writing and drawing with either hand are intact, indicating bilateral motor representation. Comprehension of both spoken and written language is intact. But information perceived or generated exclusively in the non-dominant, right hemisphere could be communicated neither in speech nor in writing; it had to be expressed through non-verbal responses. Likewise, the separated minor hemisphere was incompetent in tasks of calculation. It is not clear whether these defects represent interference with the afferent side of the speech centers or with more basic language functions of the dominant hemisphere. And if specific anatomical structures or fiber pathways cannot be identified, it is possible that more elaborate macromolecular recognition mechanisms or novel transmitters and more complex synapses underlie the advanced cognitive functions required for language.

The model of language as a species-specific universal behavioral phenotype was extended by Fox (104) to other species-specific "units" of behavior — kinship, courtship, and marriage arrangements; political behavior; associations of men which exclude women. Presumably there are definite limits to what the human species can do, to the kind of societies or cultures it can operate. No language seems conceivable that would violate the generative grammar rule of the universal language and be interpretable to man. Similarly, Fox argues that any behavioral patterns that were "gibberish" in terms of man's biological limits would cause a breakdown in social communication and be rejected. When infant baboons are raised in a zoo, they tend to mature and produce a social structure with all the elements found in the wild. Presumably, if a group of men and women were put into an experimental Garden of Eden without rules, they would produce a culture with the same basic properties as ours. The notion that we have a "wired-in" information processing capacity that responds specifically to certain kinds of inputs and responds with an element of timing in the life cycle (developmental stages) is consonant with the interactionist hypotheses of Piaget (105) for general development of cognitive processes. It is conceivable that the evolutionary development of language reflected an analogous interaction of biological potential and cultural inputs. Two million years ago, ancestral men with brain sizes little larger than that of gorillas (then or now) were hunting, building shelters, making tools, treating skins, living in base camps, with well-established bipedalism and human dentition. Under presumed selective pressures for cultural adaptation and social communication, there may have been significant increase in the relative size, complexity of connections, and variety of transmitters and recognition molecules in the evolving neocortex. It is likely that our brains contain not only the capacity for culture, but also determine the forms of culture, through some universal grammar for both language and general behavior.

We may over-emphasize the differences between culture and instinct. Stereotyped, instinctive mechanisms are highly efficient, but dangerously rigid. Ants can have societies but not politics. Politics occurs only when members can change places in a hierarchy as a result of competition, as in gregarious, terrestrial primates. Yet, much of our behavior is "unconscious" or "automatic" in response to common environmental and developmental inputs - an iceberg of assumptions, values, and habits, plus the impact of the conscience or super-ego reflected in a sense of guilt, of having broken taboos or rules of the tribe. The capacity for imaginative thought and the need for self-control seem to have evolved biologically and culturally together. To what extent such features have become fixed in the biology of the species in the relatively short evolutionary time of man and to what extent they represent learned behavioral patterns remains controversial.

The written forms of language introduce additional considerations. It is remarkable that after 30,000 years or so of spoken language iconic or hieroglyphic languages appeared in the short period of 2500 years in such widely separated peoples as the Sumerians, the

Chinese, and the American Indians (4300 to 2000 BC). Then the Phoenicians and Hebrews and others adopted an alphabetized language. It is not clear whether these forms of written language are significantly different or whether any more nearly iconic written language has been transformed directly into an alphabetical one. Certainly Chinese characters can be used to express complex thoughts as well as any other language.

With the knowledge of man written into books, microfilm, libraries, and computers, the species has what might be called a "superbrain" (7). Presumably a fertile group of men and women, a library, and materials would be sufficient for the reconstruction of human culture after a holocaust!

THE IMPACT OF EVOLUTION OF MAN'S CULTURE UPON MAN

When we realize that agriculture has been a part of man's life for only 10,000 years, that urbanization began some thousands of years more recently, that industrialization is a phenomenon of the past few hundred years, we must admit that the pace of change in man's environment completely overwhelms the time scale of biological, evolutionary processes. On the other hand, we find it difficult to evaluate whether or not such differences in life style require any remarkable change in the behavioral potential, the cognitive and affective functions of man. The possibility of selection is present, but its impact now must be small. Earlier development of man, by contrast, may have been dramatically enhanced by the drastic environmental changes of four successive periods of glaciation during the last million years of the Pleistocene epoch. Homo erectus (Pithecanthropus) and Homo neanderthalensis flourished during early interglacial periods and perished during glacial periods. Periodic decimation to small effective population size may have been crucial to the emergence of Homo sapiens. Now the number of our species has reached so high a level that the chance of any newly acquired hereditary traits being selected and fixed as a new species characteristic is small. In addition, the long generation time of man decreases the probability of significant change even further. It is not unlikely that we represent an evolutionary dead-end.

We may wonder how fragile our culture may be. Remarkable human civilizations in Egypt, Babylonia, Rome, and Greece all but vanished. Political turmoil anywhere seems to diminish cultural values and functions. Likewise religious dogma can be repressive; orthodox Christian ideas suppressed scientific inquiry for 1500 years. It is not clear whether the renewal of complex human culture should be attributed to lack of destruction of parallel civilizations at different stages of development or to basic capacities of remaining members of the species. All of these events, of course, occur in times that can mean little to the biological evolution of man. Another kind of example is the successful return of European Jews to an agricultural life on a kibbutz in Palestine after some 2000 years of urbanized existence.

The technology of our culture raises special possibilities. Man need not be dependent upon natural selection and upon the chance occurrence of mutations, so few of which might be advantageous. Artificial selection conditions and directed changes in the genome are present-day fascinations in the imaginative mind of man; they may become practical possibilities, intentionally or accidentally, in the future. We must understand much more of the "units" of behavior and their genetic and biochemical mediation to rationally devise any purposeful alteration of man's behavioral potential. Yet we know that non-random mating with regard to intelligence and to a variety of social factors has occurred for a long time; probably Gottesman and Heston in the morning session will deal with this issue in regard to intelligence. Non-random mating is practiced on a huge scale by man. Other current practices, such as exposure to possibly mutagenic agents in the form of environmental pollutants, drugs, and radiation, can have little short-term positive genetic impact, for the reasons of population size and generation time given above. Their potential for negative impact becomes increasingly great with further population crowding. Such environmental agents represent very much more powerful dysgenic forces than the matter of medical care for life-threatening illnesses that improves reproductive potential of these individuals. Ironically, the disease usually chosen to represent the dysgenic effects of modern medical care is diabetes mellitus, in which insulin therapy can carry patients with juvenile onset of the disease through the child-bearing period. The irony is derived from the hypothesis of Neel (106) that diabetes may have represented a "thrifty" genotype in hunting and gathering societies, where food intake was more erratic and where delay in metabolism of carbohydrates and in mobilization of fat stores might have been protective against periods of poor food supply. It is interesting that American Indian tribes have exceedingly high prevalences of diabetes mellitus. Thus, diabetes might be a "disease" once favored by selection and rendered detrimental by "progress"!

Also, it is man and his way of life that made malaria an important disease and led to selection of sickle-hemoglobin, thalassemia, and G6PD deficiency in populations where malaria was prevalent (107). Livingstone (108) traced these events to the "slash-and-burn" agriculture which opened the forest floor to stagnant pools. Such "technological advances" brought man into contact with the insect vectors of malaria; similarly, snails and rodents were attracted to settled populations and brought other epidemic diseases. The practice of single-crop agriculture also brought risks, since each cereal has its own limiting amino acids and propensity to protein undernutrition and endemic dysentery. Perhaps the most unusual vector for a specific disease is the culturally-based occurrence of kuru in the Fore language group of New Guinea, a slow-virus-caused degenerative disease of the nervous system contracted only by the cannabalistic practice of eating tne brains of worthy dead males.

In our society, the major cause of death in the child-bearing years is accidents. We might direct some attention to the predisposing factors in fatal accidents (clumsiness, epilepsy, aggressiveness, alcoholism, etc.) and test for disproportionate gene frequencies among those who are victims and instigators of the accidents.

Many models of cultural evolution exist in the products of our society, including some which may be viewed as technological extensions of central nervous system functions (Table 13). In fact, discussions of the evolution of the two-wheeled bicycle (7) and of the MG B auto (109) have been published! Of these, the computer bears the greatest interest, both for its simulation of human deduction and for the possibility that models could be devised which would undertake some kinds of synthetic, inductive "thinking" processes.

There is a potent desire in man to expand his awareness, his consciousness, his utilization of his brain's potential — by religious experience, by use of drugs, by determined intellectual effort. We have little basis to assess how nearly completely that potential is realized or to compare how different individuals do so. Table 14 lists some approaches of genetic engineering and electrical and pharmacological manipulation that have been discussed in this context.

Some biologists, evolutionists, and philosophers view the nature of man and of his consciousness as a complexity beyond human understanding (110). While total understanding may not be possible, the potential to increase our knowledge of human behavior by both reductionistic analysis of brain function and integrative, comparative study of complex behavioral correlates offers excitement and challenge for the experimental exploration of the function and evolution of the nervous system.

TABLE 1

COMPARISON OF BIOLOGIC AND CULTURAL EVOLUTION.(10)

	Biologic evolution	Cultural evolution
Mediated by	Genes	Ideas
Rate of change	Slow	Rapid and exponential
Agents of change	Random variation (mutations) and selection	Usually purposeful. Directional variation and selection
Nature of new variant	Often harmful	Often beneficial
Transmission	Parents to offspring	Wide dissemination by many means
Nature of transmission	Simple	May be highly complex
Distribution in nature	All forms of life	Unique to man
Interaction	Man's biology requires cultural evolution	Human culture required biologic evolution to achieve the human brain
Complexity achieved by	Rare formation of new genes by chromosomal duplication	Frequent formation of new ideas and technologies

TABLE 2

EVOLUTION OF MAN

Mean Brain Volume	Time Scale Years Ago	Generations Ago	Tool Use	Life Style	Arts & Language
400-550 cc	1.7 million	85,000	Simplest stone & bone	Hunting & gathering	
900 cc	600,000	30,000	More refined stone tools	Similar	
1300 cc	50,000	2,500	Stone Axes	Still hunters	Cave Painting Early languages
	30,000 10,000 8,000	1,500 500 400	Metal Tools	Agriculture	Hieroglyphic, Iconic written languages
	6,000	300	More complex tools & vehicles for transportation	Cities & agriculture	Alphabetized languages
	3,500	175			
	300	15	Complex machinery	Industrialized centers	Printing
	30 20	1	Nuclear energy use Computers	Atomic age Post-industrial Age of Aquarius	Radio, TV

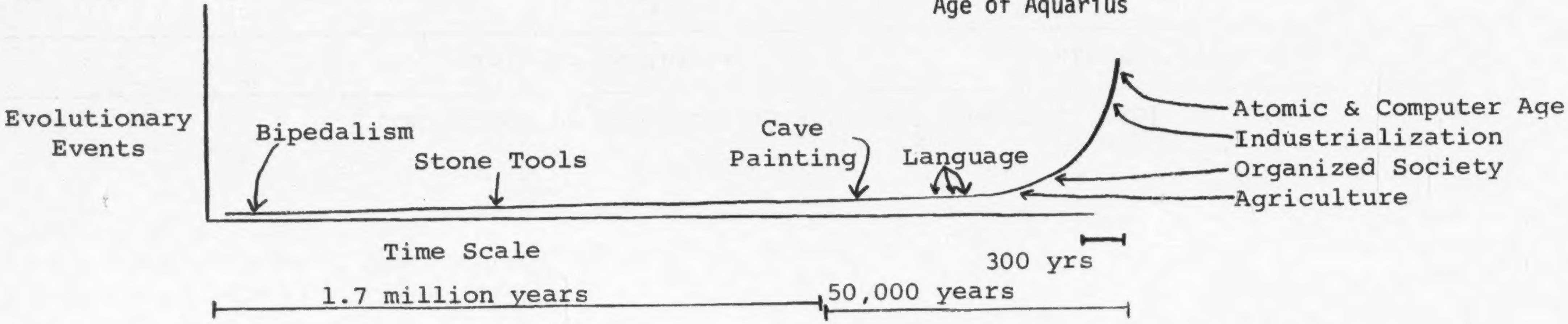
Evolutionary Events
Bipedalism
Stone Tools
Cave Painting
Language
Atomic & Computer Age
Industrialization
Organized Society
Agriculture
Time Scale
300 yrs
1.7 million years
50,000 years

TABLE 3

RATES OF EVOLUTION OF HOMOLOGOUS PROTEINS (14)

Protein and Species	Differences/Total Residues	Years of Divergence (paleontological)	Years/Mutation/ 100 Amino Acids
Hemoglobin: α-chain (horse/human)	17/141	130×10^6	22×10^6
Hemoglobin: α/γ (human)	88/146	635×10^6	
β/γ (human)	40/146	290×10^6	
β/δ (human)	8/146	58×10^6	
Cytochrome C (horse/human)	12/104	130×10^6	22×10^6
Fibrinopeptides A&B(sheep/ox)	17/40	15×10^6	0.7×10^6
Ribonuclease (Sheep/ox)	3/124	15×10^6	12×10^6

TABLE 4

ANATOMICAL FEATURES OF HUMAN BRAIN EVOLUTION

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1. Absolute increase in brain size: 400-550 cc to 1300 cc.*
2. Relative increase in forebrain } social & linguistic skills
3. Relative increase in cerebellum (3-4X) } hand skills
4. Regression of olfactory structures
5. Appearance of fetal ganglionic eminence
6. Slower maturation rate for neurogenetic processes

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*Typical brain sizes represent samples from a probable range of sizes in any given population or time.

TABLE 5

COMPARISON OF SOME MAMMALIAN BRAINS (42)

	Man	*Chimpanzee*	*Macaque*	*Indian Elephant*	*Cat*	*Rat*	*Mouse*
Weight of entire brain (gms)	1400[a]	435[b]	80	4717[c]	25	2·4	0·2
Ratio of brain weight to body weight	0·02[d]	0·007	0·05	0·0015	0·008	0·005	0·015
Area of the cortex of one cerebral hemisphere (mm^2)	90,172	24,224	6940			16	
Ratio of the area of cerebral cortex of one hemisphere to weight of body (mm^2/gm)	0·8	0·4	0·23			0·04	
Number of cells in mm^3 of cortex	10,500[e]		21,500	6,900	30,800	105,000	142,000
Volume of largest pyramidal cells (Betz cells) (μ^3)	113,400				24,112		

Information derived principally from Blinkov and Glezer, *The Human Brain in Figures and Tables*, Basic Books Inc., 1968.

[a] This is an average value. Some human brains are very much smaller. Nanocephalic dwarfs, for example, always have extremely small brains. This type of dwarf remains perfectly proportioned though seldom attaining a height of more than three feet. In consequence their brains never exceed about 400 gms in weight. These individuals are nevertheless able to master the rudiments of human speech, an accomplishment no pongid has so far achieved.

Microcephalics, like the Bantu brothers mentioned in the text, grow to a normal adult stature whilst retaining very small brains. Clearly these individuals possess a very low brain to body ratio. Once again, however, rudimentary speech and other social accomplishments are developed.

[b] The largest pongid brain yet recorded is that of a gorilla weighing some 750 gms (Holloway, 1968).

[c] The largest brain of all is that developed by the blue whale *Balaenopterus musculus*. This weighs some 6,800 gms. It is, however, situated in a body weighing about 5,800 kgms and thus the brain/body ratio is rather low.

[d] This is probably not a very significant parameter as different animals are built of rather different proportions of fat, connective tissue, bone, etc. The ratio will also vary considerably with the age of the animal.

[e] **This number provides an indication of the volume of cortex remaining for the ramifications of nerve cell processes.**

TABLE 6

GENETIC MARKERS IN HUMAN BLOOD

Seventeen blood genetic systems listed in order of their usefulness (i.e. MNSs is the most useful) for distinguishing between two random samples of blood from western Europeans. Parentheses denote the antigens tested in a given system. The Inv and lipoprotein systems are omitted because of limited availability of reagents for testing blood specimens. The figure at the bottom of the third column indicates that less than one in 350,000 people would be expected to have the same combinations of phenotypes in these 17 systems. (83)

Genetic System	Probability that two randomly selected people have the same phenotype	Combined probability
MNSs	0.16	0.16
Rh($\mathrm{CC^{w}cDEe}$)	0.20	0.032
ABO($\mathrm{A_1A_2B}$)	0.33	0.011
Acid phosphatase	0.34	0.0037
Kidd($\mathrm{Jk^{a}Jk^{b}}$)	0.38	0.0014
Duffy ($\mathrm{Fy^{a}Fy^{b}}$)	0.38	0.0005
Haptoglobin	0.39	1.95×10^{-4}
Gm(1,5)	0.40	7.8×10^{-5}
Gc	0.45	3.5×10^{-5}
PGM	0.47	1.6×10^{-5}
Lewis ($\mathrm{Le^{a}Le^{b}}$)	0.57	9.3×10^{-6}
P($\mathrm{P_1P_2}$)	0.67	6.2×10^{-6}
Adenylate kinase	0.82	5.1×10^{-6}
Pseudocholinesterase,$\mathrm{E_2}$	0.82	4.2×10^{-6}
Kell (Kk)	0.84	3.5×10^{-6}
Lutheran ($\mathrm{Lu^{a}Lu^{b}}$)	0.86	3.0×10^{-6}
6PGD	0.92	2.8×10^{-6}

Use of histocompatibility and Lp antigens and new red cell enzyme polymorphisms decreases the combined probability by another 4 orders of magnitude.

TABLE 7

ESTIMATE OF NUMBER OF PROTEIN POLYMORPHISMS IN MAN

Total nucleotide pairs in haploid human chromosome set	3 billion
Maximum number of genes (1 gene per 1000 nucleotide pairs)	3 million
Probable number of structural genes (2% of DNA)	60,000
Probable number of polymorphic genes (30% of structural genes)	20,000
Number of human polymorphisms known:	
15 serum protein variants	
11 red cell protein variants	
16 blood group antigens	42
Per Cent of Polymorphic Genes Discovered (42/20,000)	0.2%

TABLE 8

STRUCTURAL VARIATION AND QUANTITATIVE ACTIVITY OF ENZYMES

Enzyme	Relative Activity of Polymorphic Structural Loci	Author(see 59)
Acid phosphatase	P^A : 100 P^B : 150 P^C : 200	Spencer et al, 1964
6-PGD	Pgd^A : 100 Pgd^B : 115	Parr, 1966
G6PD	Gd^B : 100 Gd^A : 80	Long, 1966
Adenylate Kinase	AK^2 : 100 AK^1 : 150	Modiano et al, 1970
Phosphoglucomutase		
Locus 1	PGM_1^1 : 100 PGM_1^2 : 100	Modiano et al, 1969
Locus 2	PGM_2^1 : 100 PGM_2^{pygmy}: reduced	Santachiara et al,1970
Galactose-1-P uridyl transferase	Gt^+ : 100 Gt^{Duarte} : 50	Beutler et al, 1966
Pseudocholinesterase		
Locus 1	E_1^u : 100 E_1^a : 50	Simpson, 1968
Locus 2	E_2^- : 0 E_2^+ : 30	Harris et al, 1963

TABLE 9

ELECTROPHORETIC SCREENING OF GLYCOLYTIC ENZYMES IN HUMAN BRAIN TISSUE

Enzyme	Buffer System	#Variant/Total Alleles
Hexokinase	TP	0/300
Phosphohexoseisomerase	TC	0/300
Phosphofructokinase	TP + ATP (10^{-4}M)	0/144
Aldolase	TEB	0/600 (2 loci)
Triosephosphate isomerase	TC	0/300
Glyceraldehyde-3-phosphate dehydrogenase	TEB + NAD_4 (10^{-4}M)	0/240
Phosphoglycerate kinase	TC	1/203
Phosphoglycerate mutase	TEB	0/300
Enolase	TP	1/300
Pyruvate Kinase	TC	0/300
Lactate dehydrogenase	PHOS	0/600 (2 loci)

Buffer systems:	TP	Tris-phosphate, pH 8.6
	TC	Tris-citrate, pH 7.5
	TEB	Tris-EDTA-borate pH 8.6
	PHOS	Phosphate, pH 7.0

TABLE 10

Clinical Correlation of Isoenzyme Data for Glycolytic Enzymes

Glycolytic Enzymes	Tissue-Specific Isozymes Occur	Deficiency Described in RBCs	
		Hemolytic Anemia	Neurologic Signs
Hexokinase	+	+	0
Phosphohexoseisomerase	0	+	0
Phosphofructokinase	+	+	0
Aldolase	+	0	
Triosephosphate isomerase	0	+	yes
Glyceraldehyde-3-P-D	+	+	0
Phosphoglycerate kinase	0	+	yes
Phosphoglycerate mutase	+	0	
Enolase	+	0	
Pyruvate kinase	+	+	0
Lactate dehydrogenase	+	0	

TABLE 11

INBORN ERRORS OF METABOLISM AND PREDOMINANT PHENOTYPE

Syndrome	Enzyme	Mental Retardation	Neurologic Dysfunction	Psychiatric Dysfunction	Intrinsic to CNS
Phenylketonuria	phenylalanine hydroxylase	++++	0	0	No
Homocystinuria	Cystathionine synthetase	0/++	(vascular accidents)	??	Yes
Histidinemia	histidase	0/++	speech impairment in half of cases		?
Maple-syrup urine disease	Branch-chain ketoacid decarboxylase	+++++	Ketotic coma	---	No
MSUD variant	(Incomplete deficiency)	0	Episodic ataxia	---	No
Metachromatic Leukodystrophy	Arylsulfatase A	0 (secondary)	Motor & Mental deterioration, age 2	---	Yes
MLD, adult form	(8 cases)	0	0 (late)	"schizophrenia"	Yes
Lesch-Nyhan	HGPRTase	+++	++++	++++	Yes

TABLE 12

VARIANTS OF THE NORMAL HUMAN EEG

Rhythm	Genetic Basis	Population Frequency	Comment
Normal Alpha(8-13 cps)	Polygenic		
Low voltage alpha	Auto Dom	7 %	
Quick Alpha(16-19 cps)	Auto Dom	0.5 %	
Occipital Slow (4-5 cps)	??	0.1 %	?Psychopathy
Monotonous Tall Alpha	Auto Dom	4 %	?Assortative Mating
Beta Waves	Multifactorial	5-10%	Sex, Age ?Ass.Mating
Frontal Beta Groups (25-30 cps)	Auto Dom	0.4 %	
Fronto-precentral Beta (20-25 cps)	Auto Dom	1.4 %	

TABLE 13

TECHNOLOGICAL EXTENSIONS OF CNS FUNCTIONS

Vision	Microscope---Telescope---photosensitive transducers
Hearing	Stethoscope---Telephone Receiver
Smell	Gas Chromatograph
Information Processing	Computers

TABLE 14

DELIBERATE MODIFICATIONS OF BRAIN AND BEHAVIOR

(based upon table of G.C.Quarton)

- I. Affecting the Development of Nervous system Structures
  - A. Genes
    - 1) Selective fertilization by genotypes
    - 2) Cloning of desired genotypes *in vitro* or in foster uteri
    - 3) Introducing genes by viral transduction
  - B. Gene Expression
    - 1) Growth factors
    - 2) Hormones
      at critical developmental periods
    - 3) Specific connections or transmitters
- II. Non-Programmatic Modification of Brains
  - A. Surgical approaches
    - 1) Grafts = additions
    - 2) Ablations = subtractions
    - 3) Reconnections
  - B. Electrical stimulation or interference, use of drugs, hormones, chemicals
    - 1) Generalized changes in efficiency
      - a) Arousal systems
      - b) Motivational systems
    - 2) Selective alteration of weighted factors in complex functions
    - 3) Input of artificial information
      - a) Selective elicitation and suppression of behavior and subjective experience
      - b) Selective reinforcement of behavior patterns
      - c) Information for memory stores
- III. Programmatic Modification of Brains
  - A. Generalized enrichment or impoverishment ("cultural milieu")
  - B. Modifying options and opportunities
  - C. Reinforcing selected behavior patterns
  - D. Shaping and selecting reinforcers
  - E. More complex learning technologies
- IV. Combinations of above with monitoring, telemetry, computer evaluation

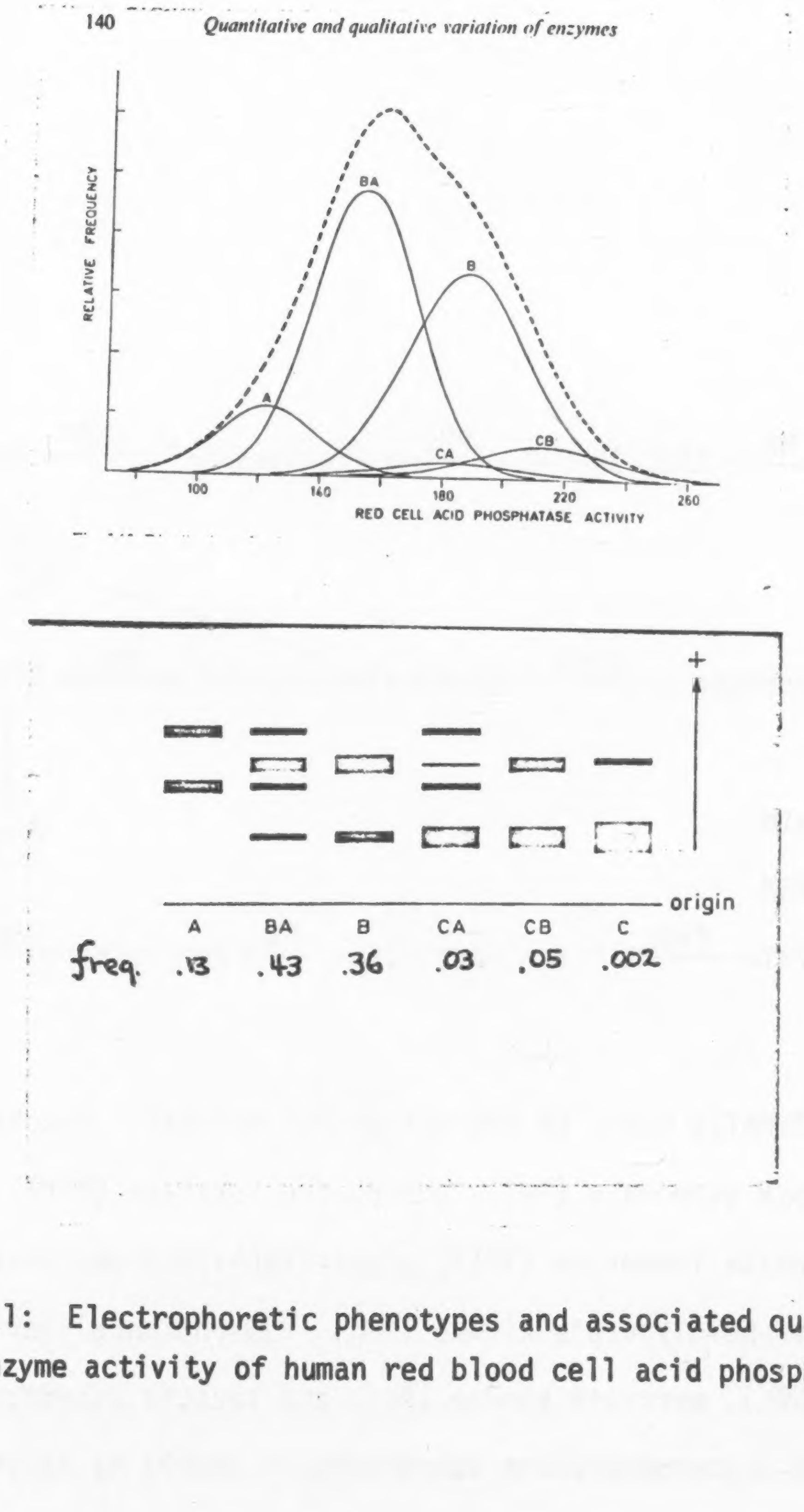


Figure 1: Electrophoretic phenotypes and associated quantitative enzyme activity of human red blood cell acid phosphatase(60).

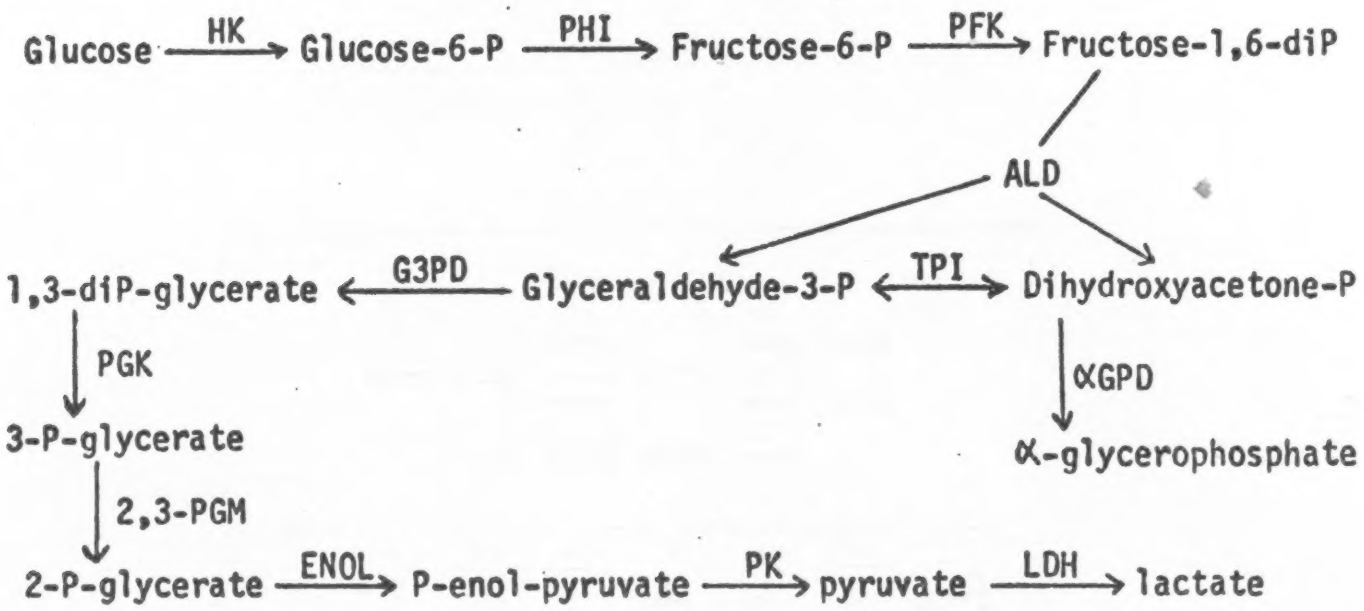
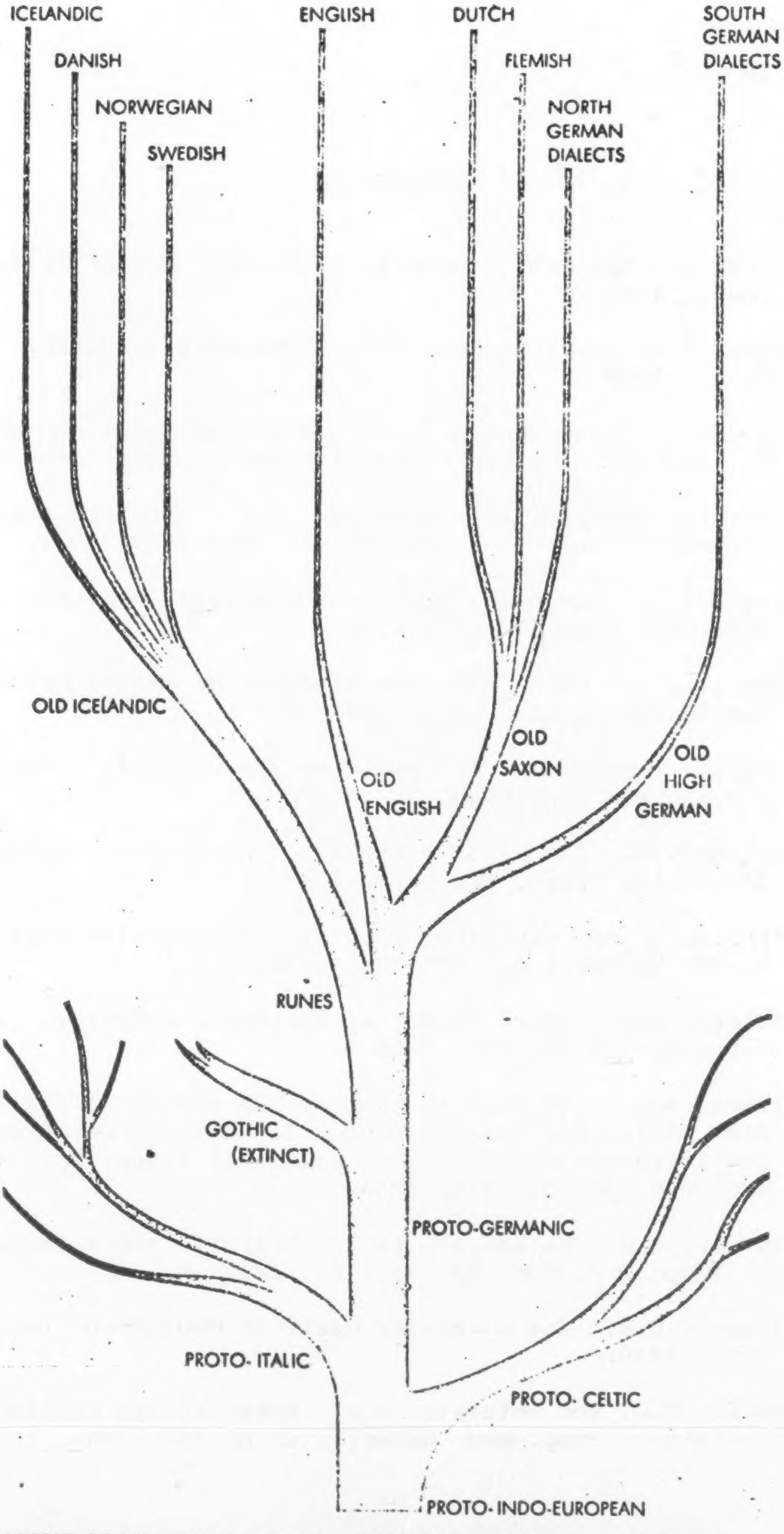

Glucose
HK
Glucose-6-P
PHI
Fructose-6-P
PFK
Fructose-1,6-diP
ALD
1,3-diP-glycerate
G3PD
Glyceraldehyde-3-P
TPI
Dihydroxyacetone-P
PGK
αGPD
3-P-glycerate
α-glycerophosphate
2,3-PGM
2-P-glycerate
ENOL
P-enol-pyruvate
PK
pyruvate
LDH
lactate

Figure 2. ENZYMATIC STEPS OF THE GLYCOLYTIC PATHWAY: hexokinase (HK), phosphohexose isomerase (PHI), phosphofructokinase (PFK), aldolase (ALD), triosephosphate isomerase (TPI), glyceraldehyde-3-phosphate dehydrogenase (G3PD), phospho-glycerate kinase (PGK), 2,3-phosphoglycerate mutase (2,3-PGM), enolase (ENOL), pyruvate kinase (PK), and lactate dehydrogenase (LDH). In addition, α-glycerophosphate dehydrogenase (αGPD) is shown.


ICELANDIC
DANISH
NORWEGIAN
SWEDISH
ENGLISH
DUTCH
FLEMISH
NORTH GERMAN DIALECTS
SOUTH GERMAN DIALECTS
OLD ICELANDIC
OLD ENGLISH
OLD SAXON
OLD HIGH GERMAN
RUNES
GOTHIC (EXTINCT)
PROTO-GERMANIC
PROTO- ITALIC
PROTO- CELTIC
PROTO- INDO-EUROPEAN

ORIGIN OF MODERN GERMANIC LANGUAGES, as indicated by this "family tree," was proto-Germanic, spoken some 2,700 years ago. Comparison of present-day languages has provided detailed knowledge of proto-Germanic, although no direct documentary evidence for the language exists. It grew, in turn, from the proto-Indo-European of 5000 B.C. Historical studies cannot, however, trace origins of language back much further in time.

Figure 3: Glottochronologic "tree" of related languages (111)

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GENETIC DETERMINATION OF BEHAVIOR (MICE AND MEN)

by

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GENETIC DETERMINATION OF BEHAVIOR (MICE AND MEN)

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1. INTRODUCTION
2. THE BEHAVIORAL PHENOTYPE
3. HYBRIDS
4. TRAIT PROFILES IN DIFFERENT GENOTYPES
5. MEASURES OF LEARNING
6. EXTREME ENVIRONMENTS AND GENOTYPES
7. MICE AND MEN
8. CONCLUSIONS

1. INTRODUCTION

Behavioral traits for which single genes and chromosomes exert a major influence so that they can be studied in segregating families in laboratory animals, and in man in pedigrees pose no great problems. However, when we turn to quantitative traits that are continuously distributed greater difficulties become apparent. The methods and techniques of biometrical genetics must be employed in their analysis; one of the main aims being to assess the relative importance of genotype and environment. In laboratory animals such as Drosophila, mice, rats, and guinea pigs, rather sophisticated experiments can be carried out to separate genotype and environment, and assess the importance of interactions between genotype and environment. The techniques of plant breeding are turning out to be of use in studying behavior in animals (Parsons, 1967a), since as pointed out by Caspari (1968), animal behavior and plant morphology are analogous in that the effects of environment are comparatively larger than for animal morphology. This is because, at the behavioral level, animals are much more environment-sensitive than at the morphological level, hence the usefulness of techniques aimed at detecting and estimating environmental effects.

One important technique is the study of inbred strains, which provide an estimate of the heritability in the broad sense. An extension of this, taken from agricultural practice, is to study a trait, behavioral or otherwise, in a number of inbred strains in a number of environments. For a behavioral trait for example, we could have a strains at b temperatures and c light-intensities, with r replicates at each temperature and light intensity. A simple analysis of variance enables the estimation of variance components of strains Va and various strain x environment interactions, Vab, Vac, and Vabc, and these can be compared with the environmental variance. Interactions of this sort could well be of importance in behavioral work, especially if extreme environments are used. Other techniques consist of taking inbred strains and studying the F_1, F_2, and backcross generations. This provides estimates of the heritability in the narrow sense. Probably the best general technique for a trait about which we have little information is the diallel cross, which is a powerful technique for a general survey of a series of strains, perhaps in several environments, whatever the aim or method used. It is an extensive analytical method rather than intensive, as a number of inbred strains and hybrids can be surveyed at once, and it permits an estimate of the heritability in the narrow sense. It has been used a number of times for behavioral traits, but usually only in one environment (for references see Parsons 1967a; Broadhurst, 1967). The other main technique, somewhat less commonly used in behavioral work is that of correlation between relatives.

The problem of obtaining estimates of genotype, environment, and of genotype x environment interaction is stressed because when we turn to man, we face immense difficulties, since for a start environments

...3

cannot generally be defined, therefore the techniques of studying a series of individuals in a series of known and defined environments is not possible. However, some information can be derived from twin studies, correlations between relatives, and the comparison of adopted and natural children. In some cases, tolerably reliable results have been obtained. (see for example Jinks and Fulker, 1970).

The object of this paper is to discuss some data on three inbred strains of mice, C57 (C57Bl), C3H, and Ba (Balb/c) and their hybrids for various behavioral measures, weight, and skeletal divergence. The results will be discussed especially from the point of view of making possible inferences about human behavior, in the hope that they will complement the more conventional biometric approach. Some of the experimental data on behavior are reported in Rose and Parsons (1970) and skeletal divergence in Howe and Parsons (1967).

2. THE BEHAVIORAL PHENOTYPE

The observations to be described were based on mice 59 days of age on the day of first observation, and the following behavioral measures were made :-

(1) Open field activity, measured as the number of squares entered in an arena in exactly two minutes. The arena consisted of an open perspex box, the floor of which was marked off into 16 four inch squares. A square was defined as being entered if all four feet are within it.

. . . 4

(2) Open field emotionality, as assessed by the sum of the number of urinations and fecal boluses deposited in the arena in two minutes.

(3) Exploratory activity, measured as the number of crossings of the central barrier in a shock apparatus in one minute. The shock apparatus consisted of a perspex box with a grid floor; the floor being divided into two equal parts by a low central barrier.

(4) Initial reaction to shock. After one minute of exploration, a light source was switched on above the apparatus and this was followed by a shock to the feet through the floor two seconds later. The shock, consisting of a 60 volt source which supplied a 250 mA current, could be applied to either side and the central barrier, the latter being shocked to prevent the mouse from "sitting on the fence". The times recorded for the first jump were used as a measure of "initial reaction to shock".

(5) Learning in the conditioned avoidance apparatus. The mouse was then rested outside the apparatus, and then given further trials. In total, the mouse received ten shock trials in the following sequence (a) four trials each one minute apart, (b) after a rest of one hour three further trials, and (c) after a rest of 24 hours three further trials. The ten trials were used to assess the ability of mice from different strains to learn to avoid shock and so provide an estimate of learning ability.

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A summary of the results obtained is presented in Table 1. In all cases C3H was intermediate, and C57 and Ba extreme, and the same was found for body weight. This shows that C57, the lightest strain, was the most active with the highest exploratory ability, and responded to shock the most rapidly and learnt best, It was also the least emotional. The Ba strain was the complete opposite for all traits, and C3H intermediate. Therefore, evidence is emerging for behavioral phenotypes corresponding to particular genotypes.

It may be of significance that there is an apparent association of weight with the behavioral phenotype, since turning to man this could support postulated associations between the behavioral phenotype and morphology. However, before turning to consider this point further, we will look at morphology as assessed by the incidence of minor skeletal variants. In mice, by the use of inbred strains and mutant stocks, it can be shown that much of the variation in skeletal morphology between strains is genetic (Grüneberg, 1952; Searle, 1954). Deol and Truslove (1957) and Grüneberg (1963) have suggested that many if not most minor skeletal variants are expressions of generalized or localized size variations. Therefore, Howe and Parsons (1967) classified skeletons of mice in the three strains for the presence or absence of 25 minor skeletal variants, consisting of 15 of the skull, eight of the vertebral column, and two of the appendicular skeleton.

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From the percentage incidences of each variant in the strains, a mean measure of divergence between strains can be obtained. The incidence of each variant p was transformed to an angular value ϕ, such that $\phi = \sin^{-1}(1-2p)$. A measure of difference or divergence between the two populations is given by

$$X = (\phi_1 - \phi)^2 - (\frac{1}{N_1} + \frac{1}{N_2}),$$

where ϕ_1, ϕ_2 are angular values corresponding to p_1 and p_2, and N_1 and N_2 are the sizes of the two populations. If a number of variants are taken, a mean measure of divergence can be computed by dividing the sum of the individual measures of divergence for each variant by the number of variants, so in this case the mean measure of divergence will be $\frac{\sum X}{25}$ (for further details, including expressions for variances see Berry, 1963). The mean measures of divergence provide a quantitative expression of the separation of populations. The method assumes that all variants have an equal effect on fitness. This is almost certainly an incorrect assumption, but it is hoped that it provides a reasonable assessment of relative divergences between populations, especially in view of some work of Truslove (1961), who found that the occurrences of nearly all the variants she studied were uncorrelated, indicating that the sensitivity of detection of differences between populations increases with the number of variants studied.

Divergences between strains indicate again that the difference between C57 and Ba is the greatest (Table 2), followed by that between C57 and C3H. The difference between Ba and C3H is considerably

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smaller than the other two comparisons, which in fact is reasonable as the Ba strain is derived from the Bagg albino strain, and the C3H from a cross between the Bagg albino and Little's DBA strain.

The similarity between weight, and pattern of skeletal variation, supports an association between the incidence of many skeletal variants and the size of structures associated with body weight. Admitting that the number of strains is limited, this naively allows one to argue for an association between genotype, skeletal morphology, weight, and various behavioral parameters. This may be reasonable, since skeletal variants are presumably associated with variants of the muscular, nervous and vascular systems, and such variants would presumably have consequences at the behavioral level.

This leads us again to the question of a possible relationship between behavior and morphology in man, as was put forward by Sheldon (1940, 1942) in his classification of individuals according to their degree of endomorphy, mesomorphy, and ectomorphy, with ratings for each dimension derived from a standardized set of photographs. Based on 200 male college students, he assigned ratings for somatotype and for temperamental variables. A considerable association between temperament and physique was found, perhaps overestimated by Sheldon, but even taking this into account, an association still occurs. It may, to an experimentalist seem rather poor to search in this way for correlations, knowing as we do that correlation does not imply causation.

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However, it seems one step better to look at such situations with the knowledge of experimental animals in mind.

Further evidence for an association between morphology and behavior comes from the genus Drosophila. Studies of behavior in this genus show that the differences in courtship between closely related species are quantitative but sizeable, but in contrast the quantitative differences between mutants within species are very small indeed, for example the courtship behavior differences between certain mutants of D. melanogaster are very small compared with the differences between the two sibling species, D. melanogaster and D. simulans. Brown (1965) quantified differences between eleven species of the obscura group for behavioral and morphological traits, by working out Mean Character Differences between all possible combinations of 11 species in pairs, based on 20 behavioral and 24 morphological traits. Although there is a certain amount of arbitrariness in the calculation of the Mean Character Differences, the correlation coefficient between the 55 possible species combinations in pairs between behavioral and morphological traits came to 0.5763 ($P<0.001$ for difference from 0), thus showing quite clearly that behavioral and morphological divergence is associated. To quote from Brown (1965) :-

"It is clear that, throughout the genus Drosophila, there is a close correlation between behavioral and morphological divergence. The differences between mutants are slight; those between sibling species are greater, and those between non-sibling species in the same division

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greater still. As the morphological divergence increases between divisions, and between groups of the same subgenus, so does that of the behavior, until in the end we find the major differences in behavior between the subgenera".

3. HYBRIDS

We have so far considered the three inbred strains of mice, but not the hybrids between them. Most traits showed dominance either towards one or other extreme inbred strain in the F_1's. However, for measures of learning in the conditioned avoidance response apparatus, heterosis was quite marked (Fig. 1). Heterosis was greatest for crosses involving one C57 parent. Hybrids from crosses between Ba and C3H tended to show a rather lower level of heterosis, probably because these two strains are more closely related with each other, than with C57. As well as showing heterosis, hybrids between inbred strains showed less variability compared with the inbred strains. In other words, the hybrids show homeostasis presumably because the processes leading to the observable phenotype are better buffered against environmental variation in hybrids as compared with inbred strains. This has been well documented in the literature for many morphological and fitness traits, and the same would be expected for behavioral traits.

If the observation of an association between heterosis and homeostasis for learning is correct, can an explanation be offered? In outbreeding species, heterosis for quantitative traits tends to be fairly

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marked for traits directly related to fitness such as viability, fecundity etc. Such traits which are direct components of fitness show considerable inbreeding depression when artificial inbreeding is carried out, because of reduced relational balance compared with the outbred situation. Under natural conditions such traits are subject to directional selection for higher fitness. In comparison, morphological traits such as weight of mice which must be subjected more to stabilizing selection are less prone to inbreeding depression, and hence crosses between inbred strains tend to yield less heterosis. Breese and Mather (1960) and Mather (1966) and others have discussed genetic architectures and their consequences under various modes of selection in some detail, and the above comments fit in with these discussions.

Of the behavioral traits in mice discussed, it seems reasonable to assume that learning would be subject to fairly intense directional selection, while traits such as activity and emotionality would be more subject to stabilizing selection. In agreement with the argument presented, is the observation that learning in the conditioned avoidance apparatus does in fact show considerable heterosis associated with homeostasis.

The reduced variability of hybrids compared with the inbred strains also represents a special form of genotype x environment interaction. The problem of genotype x environment interaction is particularly difficult to deal with for behavioral traits as already pointed out. In particular, if such interactions are most marked for those traits

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related to fitness, i.e. subjected to directional selection, which in our example presumably consist of traits with a learning component, there are real problems in extrapolation to man. It is precisely these sorts of traits which are studied most in man especially by psychologists, and if these are those with the greatest problems so far as genotype x environment interactions are concerned as suggested, we face problems of acute difficulty in man where neither genotype nor environment can be controlled. On the other hand, simpler traits say of a sensory perception nature might well be subjected to less intense directional selection if not stabilizing selection, and are probably more amenable to accurate study, both in mice and men.

This is not to say that heterosis associated with homeostasis does not occur for other traits; thus Bruell (1964a, b) reported on data in mice for 31 hybrids derived from 11 inbred strains for wheelrunning and exploratory behavior, both traits presumably having a lower component of learning than conditioned avoidance learning. Of the hybrids, 18 were derived by crossing unrelated parents, nine by crossing related inbreds, and four by crossing inbreds belonging to sublines of C57 mice. It is clear that heterosis is general in both sexes for wheelrunning when unrelated strains were crossed (Table 3), and less general when related strains and sublines were crossed, presumably because crosses between related strains and sublines led to rather homozygous individuals, showing less relational balance than for crosses between unrelated strains.

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As well as showing heterosis, the hybrids often showed less variability as assessed by coefficients of variation compared with the inbred strains, thus they showed homeostasis. Homeostasis is most common in crosses between unrelated individuals and least frequent in the sublines (Parsons, 1967b). In other words there is an association between heterosis and homeostasis (Table 3c). Certain other published data on other traits show an association between heterosis and homeostasis (see Parsons, 1967b). The same strains were tested for exploratory behavior (Bruell, 1964b), as assessed by placing mice individually in a 4-compartment maze. As a mouse moved from one compartment of the maze to another, it interrupted a light beam and activated a photorelay and counter. The exploration score of an animal consisted of the total count registered in ten minutes of counting. Heterosis and homeostasis were found more often than not, but less so for wheelrunning, therefore it is not surprising that no real association between homeostasis and heterosis was found.

While these data show, especially for wheelrunning, an association between heterosis and homeostasis, it is difficult to make comparisons with the data of Rose and Parsons (1970) since in the latter data (1) a gradation of traits with increasing learning components was employed, (2) different genotypes and behavioral tests were used as compared with Bruell. Therefore, at this stage, the suggestions made about the association of heterosis with associated homeostasis for traits measuring learning, should remain as a working hypothesis only.

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It must be stressed that inferences about the genetic architecture of traits may well depend on the sample of strains used; a principle frequently put to one side in quantitative genetic theory, but a principle which should lead us to be as equally cautious about results agreeing with a given hypothesis, as those disagreeing with it. The dependence of results on the degree of relatedness of strains shows this to some extent. Thus we can conclude that for a given series of inbred strains and hybrids, a result showing heterosis associated with homeostasis, was found for traits with learning components, as opposed to traits with little or no learning component. This result based on the given series is probably meaningful, although of course it needs to be extended further.

4. TRAIT PROFILES IN DIFFERENT GENOTYPES

Guttman (1967) compared the correlations between ridge counts of the fingers of an English sample with those of the Parsis of India. He found that in both cases the adjacent fingers (except the thumb) are more highly correlated than those further apart. In other words, correlation matrices from both populations show the same pattern, indicating developmental relationships of related measures. A general relationship was also found, for example, for bone lengths in several animal species. Even where the cause of the relationship is unknown, the presence of such constancies is highly suggestive of an underlying similarity of the population samples with respect to the variables forming the pattern. For mental tests, cross-cultural stability was found for American College students, and for Chinese students studying at

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American Universities. The same was found for some sensory variables (hand-preference, arm-folding, and hand-clasping) for five Israeli sub-populations, even though the actual incidences of these variables differed between groups. Therefore correlational patterns are frequently similar in different groups.

The mouse data provide us with five measures where simple observations were made on all individuals, namely weight, open field activity, open field emotionality, exploratory activity, and initial reaction to shock. Correlation matrices are given in Table 4 for the inbred strains and hybrids. There is a general positive association between open field activity and exploratory activity for all strains as would be expected. For these two traits, which are essentially activity measures and initial reaction to shock, negative correlations within inbred strains were found, in particular for Ba. Thus within the Ba strain, the most active mice in both the arena and shock apparatus are significantly better at escaping from shock than are the less active mice.

So far as similarity of correlation matrices between inbred strains and hybrids are concerned, since most coefficients do not differ significantly from 0, there is less pattern than in most of Gutman's examples. However, it can be said that there tends to be a similarity for those contrasts where significant results were found. Another point is that there are only two correlation coefficients significant at $P<0.05$ for hybrids out of a total of 30 calculated. In contrast, strain Ba shows three significant results, two at $P<0.01$ and one at $P<0.05$, and in

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general the deviation from 0 of values for inbreds exceeds that of the hybrids (even disregarding C3H where rather few mice were classified). Looked at in another way, in the inbreds there are seven and in the hybrids two correlation coefficients > $|0.24|$. Thus it seems that the hybrids show less extreme associations between traits than the inbred strains. Since within inbred strains and hybrids, we are presumably dealing with identical genotypes, this provides further evidence for greater stability of hybrids or homeostasis. It represents a form of genotype x environment interaction analogous to the lower variability of hybrids for learning traits as discussed in the previous section. From the genetic architecture point of view, the hybrids would approximate more to the situation in man being an outbreeding species. This leads us to another difficulty in studying human behavior, in that compared with animals, it is not possible to study extreme genotypes from which inferences may be made, which may throw light on less extreme genotypes. The fact that one cannot carry out selection experiments in man is another manifestation of this problem.

5. MEASURES OF LEARNING

In the conditioned avoidance apparatus at trial 2 (T2), C57>Ba, C3H in learning ability, Ba and C3H being almost equivalent (Fig. 1)/ At T4, however, C3H>C57>>Ba. Thereafter Ba was always the poorest at learning, but C3H tended to drop in learning ability after a rest (at T5 and T8), whereas C57 did not. All of these observations represent genotype x environment interactions, since the ordering of genotypes varies according to trial number, although overall C57 was just superior to C3H, which were both definately superior to Ba as already pointed out. This result also suggests that the learning component of the behavioral phenotype may not fit in quite as well as previously indicated with simpler forms of behavior and with morphology (as in Table 1). This became first evident with the heterosis found for learning, which was not shown for the other behavioral traits under study.

This leads to a further problem for traits associated with learning, since a measure of learning different from that used so far is the percentage of no shock jumps, or the percentage of trials where the mouse jumped to the safe side of the apparatus after the light signal was switched on, but before the shock was applied. Trials 2 to 10 were used to assess this, trial 1 being omitted because any crossing of the barrier before experiencing the shock cannot be regarded as a conditioned avoidance response. The highest proportion of no shock jumps occurred for trials 4, 7, and 10 i.e. at the end of each set of trials, thus showing learning during each set of trials. This was followed by a lower percentage following the first trial after resting as might be expected. The overall superiority of the genotypes was

C3H > C57 > Ba,

in contrast with the measure of learning previously discussed, measured as the average time for all jumps. Thus C3H and C57 are reversed for the two measures, and show that different rankings may occur according to the mode of assessing learning.

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Therefore we face two problems in mice for learning :-

(1) genotype x environment interactions between trials, and

(2) variable results according to the mode of assessing learning.

Considering man, the Stanford-Binet I. Q. test is commonly used as a measure of intelligence, but questions have been asked as to its suitability in all cultural situations (i. e. environments) and populations. Furthermore, it can be debated as to the degree to which different measures of intelligence give the same relative results between populations. The mouse results are difficult enough to interpret, and show clearly that extrapolation to man is peculiarly difficult for traits associated with learning.

In conclusion, in spite of the results in Table 1 showing an association between morphology and the behavioral phenotype in mice, it seems from a more detailed consideration, that this association does not necessarily hold for learning. In man, therefore, it seems likely that there would be little real association between somatotype and intelligence, but on the other hand, it would be expected that somatotypes may be associated with traits of lesser complexity from the behavioral point of view, such as those more directly associated with the skeletal, muscular, and vascular systems, which would be traits more of a sensory-perception type.

The mouse data referred to so far were all collected at a standard age, however, some data were collected at younger ages. These

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data generally showed for all genotypes that weight increased with age as did emotionality, but that activity decreased with age. This is just the type of relationship in Table 1 between genotypes, as compared with that between environments (ages) in this case. The same situation was found for litter size, since mice from litter sizes < 6 were less active and heavier than those from litter sizes $\geqslant 6$, although there seemed to be no trend for emotionality (Rose and Parsons, unpub.). In other words, for these traits there seems to be some association between behavior and morphology, but in this case as a result of environment, rather than genotype.

For traits associated with learning, the situation again seemed more complex. Young mice showed a lower initial reaction to shock, but there was no litter size effect. Conversely, for the percentage of no shock jumps there was a litter size effect since the percentages were highest for litter sizes $\geqslant 6$. For conditioned avoidance learning generally, over the 10 trials, litter size was found to have no consistent effect, but there seemed to be an age effect in that younger mice tended to forget easier, especially after a long break (24 hours), but the effect was hardly significant. Once again therefore it seems difficult to say there is an association between morphology and traits with a high component of learning, although of course in this case morphology is altered by environmental means.

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6. EXTREME ENVIRONMENTS AND GENOTYPES

The importance of extreme genotypes in studying a trait in experimental animals has been stressed frequently. This in outbred species the use of inbred strains, or of individuals which have been selected for extremes for a trait is common for quantitative traits including behavioral traits (Parsons, 1967a), and this approach is illustrated for inbred strains in mice in this paper. The approach of studying extreme genotypes, in the sense of being largely homozygous is not of course possible in man; since we have to work on the available population.

The geneticist, preoccupied with studying various genotypes, many being extreme in experimental animals, seems to have paid less attention to the question of environmental variability, being mainly concerned with keeping the environment constant and often optimal in experimental organisms. There are exceptions mainly in the area of plant breeding and in experimental work on some species of Drosophila. For example, in population cages of D. pseudoobscura, heterokaryotype advantage occurs at the more extreme temperature of 25°C as compared with 16.5°C (Dobzhansky, 1948). Other examples of heterokaryotype advantage in extreme environments in Drosophila include cold tolerance, mating speed and duration of copulation at high temperatures, and desiccation. Similarly, hybrids between inbred strains and other homozygotes tend to show an enhancement of heterosis in extreme environments in several species of Drosophila, mice, and plants such as

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Arabidopsis thaliana, Nicotiana rustica, and maize (see Parsons, 1971; Parsons and McKenzie, 1971 for references). Such extreme-environment heterosis has been postulated to be associated with temperature sensitive and correlated enzymes, or the general poorer fitness of homozygotes compared with the corresponding heterozygotes, because of the breakdown of relational balance in the heterozygotes in forming homozygotes. It was postulated that extreme-environment heterosis could provide an explanation of the high level of polymorphism in natural populations, additional to those already advanced in the literature, since it would not imply a high genetic load under relatively optimal environments. This again represents an example of genotype x environment interaction, since in moving the environment from optimal to extreme, the hybrids change relatively less than the homozygotes, leading to the observed homeostasis across environments for heterozygotes.

Because of the concentration of attention on genotypes, the study of behavior under extreme environments has been rather neglected. In Drosophila the types of extreme environments that can be studied include extremes of temperature, desiccation, and competition. Rodents, however, being closer to man phylogenetically seem to be worth detailed study. Cooper and Zubek (1958) studied two lines of rats in which genetic differences in the rat's capacity to find their way through a maze had been accumulated by artificial selection, leading to maze "bright" and maze "dull" rats under a "normal" laboratory environment. Under a "restricted" environment, no differences between lines were

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found and both behaved at the same low level. Conversly in a "stimulating" environment, there was a much larger improvement in the maze "dull" than the maze "bright" mice. As pointed out by them and by Bodmer and Cavalli-Sforza (1970), this could have implications in the determination of human I.Q. in restricted and stimulating environments. Manosevitz and Lindzey (1970) studied hoarding in various inbred strains in an enriched and standard environment, and found substantial strain x environment interactions. They also studied hoarding in a stress situation which involved a 10-second immersion in room temperature water 15 to 20 minutes before each daily trial. The general magnitude of the effect of treatment in the F_1 and F_2 generation was less than in the inbred strains themselves, which is not surprising in view of the evidence for the greater stability of heterozygotes as discussed above. Other extreme environments in mice could consist of extreme crowding, and extremes of temperature, both high and low. It is, for example, known that under crowded conditions adrenal weights are high (Davis, 1966). A large adrenal gland leads to a high level of certain hormones which have the effect of lowering reproductive rate. Such changes tend to regulate the population size. It is interesting too that the increase in adrenal weight occurs when numerous aggressions occur because of high population density, and there is evidence for the same sort of situation in rabbits (Myers, 1966). Comparisons of different inbred strains and hybrids could well provide information on genotype x environment interactions in mice of some importance, and perhaps similar studies would be worth doing in mice collected from different populations in the wild, which would represent genetically more the situation in human populations.

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In the same way, because of the difficulty of studying extreme genotypes in man, the study of behavior under extreme environments could be worthwhile, especially if associated with various physiological and biochemical tests. Extreme environments could include the influence of drugs, alcohol, and temperature. Even so, we cannot go as far as in animals, since differential mortality frequently has been observed in animals. Some of the issues discussed in this paper may be advanced by an approach of this sort, e.g. behavior under optimal and extreme environments in relation to socioeconomic class. The same could be studied in relation to somatotype and might provide additional information on the possible relationship between somatotype and behavior. Correlation matrices under optimal and extreme environments would be of interest; quite likely levels of correlation might be lower under extreme environments. Overall comparisons between ethnic groups would be of interest, because of known differential effects of certain drugs and presumably other environments on behavior in different ethnic groups. Generally, such studies could lead to the building up of behavioral phenotypes under a multiplicity of environments, and this would initially probably be most successful for sensory-perception traits. It would also seem that additional insight could be obtained by carrying out parallel experiments in mouse and man simultaneously.

7. MICE AND MEN

a. Morphology and behavior.

Sheldon (1942- see section 2) discussed possible relationships between the somatotype and behavior. In spite of the high correlations

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he found, few further studies have been carried out (see Lindzey, 1967), and in fact Lindzey pointed out that there has been a reluctance of some psychologists to give serious consideration to the study of morphology and behavior :-

> "The modal emphasis among psychologists in America has been upon learning, acquisition, shaping, or the modification of behavior, and not upon those aspects of the person and behavior that appear relatively fixed and unchanged".

Some associations between behavior and morphology can be cited in man. Thus the frail ectomorph cannot be expected to employ physical or aggressive responses with the same effect as the robust mesomorph, in other words height, weight, and strength put limits upon the adaptive responses an individual can make in a given environment. In women at least, linearity (ectomorphy) is negatively associated with the rate of physical and biological maturation. Individuals who are physically extreme in some sense such as being excessively fat or thin, will be exposed to a somewhat different set of learning experiences than someone who is more modal physically or extreme in some other way. It should be pointed out that modality will vary between ethnic groups.

An extremely striking set of examples comes from data on the somatotypes of athletes (Carter, 1970). Thus almost all groups of championship athletes are rated high on mesomorphy, but the most mesomorphic are weight lifters, followed closely by Olympic Game track

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and field throwers, football players, and wrestlers. The least mesomorphic men are the distance runners. Women range from the track and field jumpers and runners, who have the lowest mesomorphy to the gymnasts who have the highest. It is also of interest that champion performers at various levels of a particular sport exhibit similar patterns of body size and somatotype, but the patterns tend to become narrower as the level of performance increases; i.e. extremes at the behavioral level correspond to extremes at the morphological level. Conversely, certain somatotypes found in non-athletes are not found at all in groups of champion athletes.

Associations between morphology and temperament have been found in students as was asserted in a striking form by Sheldon (1942) with a very high correlation. This has been confirmed more recently at a rather lower level of correlation (Child, 1950; Parnell, 1958; Walker, 1962; Lindzey, 1967). Amongst individuals showing criminal behavior, a number of surveys have shown an excess of mesomorphs (see Eysenck, 1964; Lindzey, 1967), and a few other suggested associations occur especially in relation to susceptibility to certain forms of disease. Several investigators (see Heston, 1970) have found somatotype to be associated with schizophrenia since mesomorphs are underrepresented among schizophrenics, and ectomorphs are correspondingly overrepresented (see also Parnell, 1958). Paranoids, on the other hand are high in mesomorphy (Parnell, 1958).

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Most morphological traits in man have a high heritability, as has been shown from twin studies and correlations between relatives (see for example Fisher, 1918; Clark, 1956; Spuhler, 1962). The situation is rather more difficult to assess for behavioral traits because of the complication of possible environmental variation, but heritabilities of a number of traits are reasonably high (see Parsons, 1967a for references). Unfortunately in man, studies on sensory-perception traits, which can be regarded as "simpler" than learning or personality, are rarer than those on learning and personality. Since in some cases, it seems likely that we may be closer to the actual genetical and physiological basis of a sensory perception trait (e.g. color blindness, taste testing), the suggestion of Haldane (1963) quoted by De Fries (1967) that qualitative (i.e. single gene) and quantitative studies should be combined in work on human populations clearly has merit. Haldane was referring to anthropometric data, but behavioral data are no different in principle. As he pointed out, this may lead to spurious correlations due to the presence of linkage disequilibria, however as an approach it seems worth exploiting further for those traits for which all members of a population can be assessed. Perhaps the result closest to Haldane's idea is the recent discovery that XYY males tend to be excessively tall and have criminal tendencies (see McLearn, 1970 for references). Other sex-chromosomes abnormalities, namely Turner's Syndrome (XO), and Klinefelter's syndrome XXY, are known to have behavioral effects associated with morphological changes, in particular of the gonads.

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In any case, whatever approach is used, the mouse data presented seem to argue for an association between morphology as assessed by weight and skeletal form, and the simpler forms of behavior, but probably not with traits involving a large learning component. In man as pointed out, it is these simpler traits for which associations would be expected to be found, which are those where far fewer studies have been carried out as compared with learning.

b. The mouse as a prototype in the study of human behavior.

The experimental data discussed, in common with much work on the behavior genetics of the mouse (see Lindzey and Thiessen, 1970) is based on artificial laboratory strains of mice. In particular, the genetic architecture of the inbred strains probably bears little relationship to that of free-living populations of mice. Laboratory mice are normally tame and easily handled compared with wild mice. Inbred strains and hybrids between them have their place in behavior-genetic research, since they enable studies to be made on traits which will provide estimates of relative genotypic and environmental control, and hence may give us indications of traits worth studying in wild mice. In other words, they provide us with hints on phenomena and relationships that could be sought in the wild. But it must be remembered that an open natural population must cope with numerous conditions to which the closed and sheltered laboratory population is not exposed, and in fact it can be expected that genotypes would be developed in the laboratory that are inferior in viability in nature, since they are not exposed to the effects of adverse and variable environments as found in nature.

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Even so, in mice, it seems that we do have a species which could yield information directly relevant to the study of human behavior. There are three main groups of mice (1) aboriginal mice, which so far as is known have never associated with man, (2) commensal mice which have followed man around the world as scavengers, and (3) feral mice which were once commensal with man, but have reverted to a more feral existance. They all belong to the one species Mus musculus, and numerous varieties within the above three groups are known. There are therefore some analogies relevant to the study of man for they represent a species divided into a number of populations, which from the morphological and coat color point of view are known to diverge. The various races of mice, inhabiting various different habitats and with presumed different behavior forms, could well provide us with a model through which inferences could be made about man. Compared with man, the added advantage is that of genetic manipulation. Little has as yet been done, but much could be done, which may be of interest in studying behavior in man thus :

(1) The behavioral profiles of races and subraces of mice could be studied, as well as the morphological and biochemical profiles.

(2) Information on mating patterns in mice could be obtained; is it random, density-dependent for certain traits, or assortative? In man, we know that mating is largely assortative (positive) for morphological, psychological, and sociological traits (Spuhler, 1962), and the same is likely for morphological traits in Drosophila melanogaster (Parsons, 1965).

(3) There is the possibility of studying different races of mice under

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given environments, which is not possible in man. The environments could be both optimal and extreme.

(4) Among other things the study of mouse populations may provide hints as to likely processes that will occur due to overpopulation, especially with regard to behavioral changes.

The possibility of studying wild mice is also stressed because the genetic architecture of wild mice must necessarily be more similar to man than the artificial inbred strains and hybrids commonly studied in the laboratory. Mice have the advantage of genetic manipulation not available in man, and being a rodent associated with man, could provide us with information relevant to man. Their populations are in fact probably more diverse, since in man aboriginal populations are rapidly disappearing. The area where they may be most deficient is in the study of learning and reasoning; being developed to their maximum in man, but at least mice are in a position to provide some information.

It seems clear that the slowly dying belief among some psychologists (Bruell, 1970) that it is possible to obtain "species-typical" estimates of behavioral parameters would be proven incorrect by such studies in mice. In man this is of course an oversimplification, since it is likely that just as different ethnic groups differ at the quantitative level for morphological features, they may differ for behavioral features. Unbiassed evidence on behavior is more difficult to obtain, because of the effects of previous experience, hence we should probably leave traits such as intelligence out of our detailed considerations at this stage. On

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the other hand, differences between groups in man are known for simple sensory processes, and curiously enough, as pointed out by Spuhler and Lindzey (1967), the decades prior to 1900 probably saw more pertinent investigations of this type than occurred in the ensuing 50 years. Spuhler and Lindzey (1967) document a number of examples of racial differences in traits such as visual, auditory, olfactory, and tactile stimuli, and variations in taste and weight discrimination. Although there may be flaws in some of these data, they do suggest the possible existance of interesting and appreciable racial differences in behavior. Less complex processes studied include taste blindness to phenylthiocarbamide PTC and color blindness which are under the control of major genes, and which vary in frequencies between racial groups in man. Arguing from evidence on blood groups and other polymorphic loci controlling serum proteins and enzymes, the differences between the racial groups can perhaps be regarded as quantitative (i. e. due to differences in gene frequencies at loci) rather than qualitative. Just as differences between races in man have been quantified based on anthropometric traits and blood groups, it is feasible that the same could be done for behavioral traits, especially for those traits measuring sensory perception. Between ethnic groups, there is a reasonable association between genetic distances for anthropometric traits and blood groups (Cavalli-Sforza and Edwards, 1964), and based on our arguments so far we would expect this to occur for the simpler behavioral traits.

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8. CONCLUSIONS

1. The methods of biometrical genetics, as applied to plant breeding in particular, allow the estimation of the effect of genotype, environment, and genotype by environment interactions for quantitative behavioral traits in experimental animals. Because of the difficulties of defining environments and dealing with known genotypes, the problem in man is much more difficult.

2. Three inbred strains of mice showed characteristic behavioral phenotypes for each strain in that strains Ba and C57 were usually extreme, and C3H intermediate. The same was found for weight, and the incidence of minor skeletal variants. The similarity between weight and pattern of skeletal variation supports an association between the incidence of many skeletal variants and the size of structures associated with weight, and naively allows one to argue for an association between genotype, skeletal morphology, weight, and behavior. This may be reasonable, since skeletal variants are presumably associated with variants of the muscular, nervous and vascular systems, and such variants would presumably have consequences at the behavioral level.

In man, this result supports postulated associations between somatotype and behavior described in the literature.

3. Most of the traits in mice showed dominance, either towards one or other extreme inbred strain in hybrids between them. These traits included open field activity, open field emotionality, exploratory activity,

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weight, and skeletal divergence. On the other hand for learning in a conditioned avoidance apparatus, heterosis was quite marked and was associated with lower variability in the hybrids compared with the inbred strains. The hybrids therefore show behavioral homeostasis for learning. Traits with a direct relation to fitness of which learning is one, are expected to be subject to directional selection for higher fitness. They would be expected to show greater inbreeding depression, and consequently heterosis on crossing inbred strains, whereas the other traits studied would probably be subjected more to stabilizing selection showing less inbreeding depression and heterosis.

The behavioral homeostasis represents a form of genotype x environment interaction. If the problem of genotype x environment interaction is most marked for those traits related to fitness such as learning, there are real difficulties in extrapolating to man where neither genotype nor environment can be controlled. Simpler traits of a sensory perception nature therefore should be more amenable to accurate study in man.

4. Correlation matrices between certain traits within strains and hybrids showed some consistency between strains and hybrids. In general less extreme associations were found for hybrids than inbred strains, showing another form of genotype x environment interaction.

5. Genotype x environment interactions were found between trials in the conditioned-avoidance apparatus, e.g. Ba and C3H tended to

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drop in learning ability after a rest whereas C57 did not. The measure of learning is relevant, since if assessed as the percentage of no shock jumps C3H is superior to C57, whereas based on the average times for all trials the reverse was found, so that different rankings can occur according to the method of assessing learning.

This points to even more complexities when attempting to extrapolate to man, e.g. comparing results of different intelligence tests under differing types of previous experience.

6. Because of these complexities, the learning data in mice do not support any real association with weight and skeletal morphology, as found for simpler behavioral traits. Similarly in man, no real association would be expected between traits with a high learning component and somatotypes.

7. In experimental animals, genetic analysis is frequently based on extreme genotypes, and less frequently extreme environments. Where extreme environments are studied, extreme genotype x environment interactions may occur such that inbred strains tend to be affected more than hybrids and extreme-environment heterosis tends to occur. It is considered that the study of behavior over many environments would be valuable in experimental animals. In man, where extreme genotypes cannot be bred, it is considered that the approach of using extreme environments should be explored more deeply and may add insight to a number of the issues raised.

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8. The study of behavior in man is therefore partly one of unravelling genotype x environment interactions, and their estimation, a problem which becomes more acute as the learning component of a trait increases. Until this problem can be approached with greater precision, progress may be difficult, but a multidisciplinary attack, in which experimental animals play a part, may lead to insight. Basically the function of experimental animals is to provide accurate and controlled data on relationships that could be investigated in man.

9. It is considered that possible associations between morphology and behavior in man should be explored further.

10. Some possible further extrapolations from mouse to man in the study of behavior are considered, especially the possibility of extensive studies on wild mice.

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TABLE 1

Order of inbred strains for behavioral traits, weight, and skeletal differences.

Open field activity	C57	>	C3H	>	Ba
Open field emotionality	Ba	>	C3H	>	C57
Exploratory activity	C57	>	C3H	>	Ba
Initial reaction to shock (order of superiority)	C57	>	C3H	>	Ba
Average time for all jumps (order of superiority)	C57	>	C3H	>	Ba
Weight	Ba	>	C3H	>	C57
Skeletal divergence	Ba	>	C3H	>	C57

TABLE 2

Mean measures of divergence and their standard deviations between inbred strains (after Howe and Parsons, 1967).

	Ba	C3H
C57	1.326 ± 0.221	1.012 ± 0.275
Ba	-	0.348 ± 0.156

TABLE 3

Wheelrunning in mice (data of Bruell, 1964a analyzed by Parsons, 1967).

a. Number of hybrids showing heterosis according to the degree of relatedness of the inbred parents.

	Relatedness of inbred parents			
	Unrelated	Related	Sublines	Total
Heterosis	35	9	2	46
No heterosis	1	9	6	16

b. Number of hybrids showing less variability than both parents (positive homeostasis, +), variability between both parents (o), and more variability than both parents (negative homeostasis, -), according to the degree of relatedness of the inbred parents.

	Unrelated	Related	Sublines	Total
+	21	15	-	36
o	9	4	5	18
-	3	1	4	8

c. The degree of homeostasis plotted against the occurrence or not of heterosis for the hybrids above.

	Heterosis	No heterosis	Total
+	30	3	33
o	15	5	20
-	1	8	9

TABLE 4

Correlation matrices between open field activity (A), open field emotionality (B), exploratory activity (C), initial reaction to shock (D), and weight (E). (Adapted from Rose and Parsons, 1970).

Strain Ba

	B	C	D	E
A	0.012	0.373**	-0.269**	0.009
B		0.085	0.160	0.044
C			-0.272**	-0.076
D				0.112

Strain C3H

	B	C	D	E
A	-0.170	0.359*	-0.181	0.085
B		-0.303	0.117	0.035
C			-0.099	0.176
D				-0.331

Strain C57

	B	C	D	E
A	-0.069	0.289***	0.084	-0.007
B		-0.046	0.006	0.093
C			-0.176	-0.112
D				-0.105

Ba x C3H

	B	C	D	E
A	0.124	0.172	0.003	-0.142
B		0.063	-0.128	-0.006
C			-0.082	0.246*
D				-0.057

Ba x C57

	B	C	D	E
A	0.010	0.270*	0.007	0.008
B		0.078	-0.118	0.122
C			0.036	0.131
D				-0.086

C57 x C3H

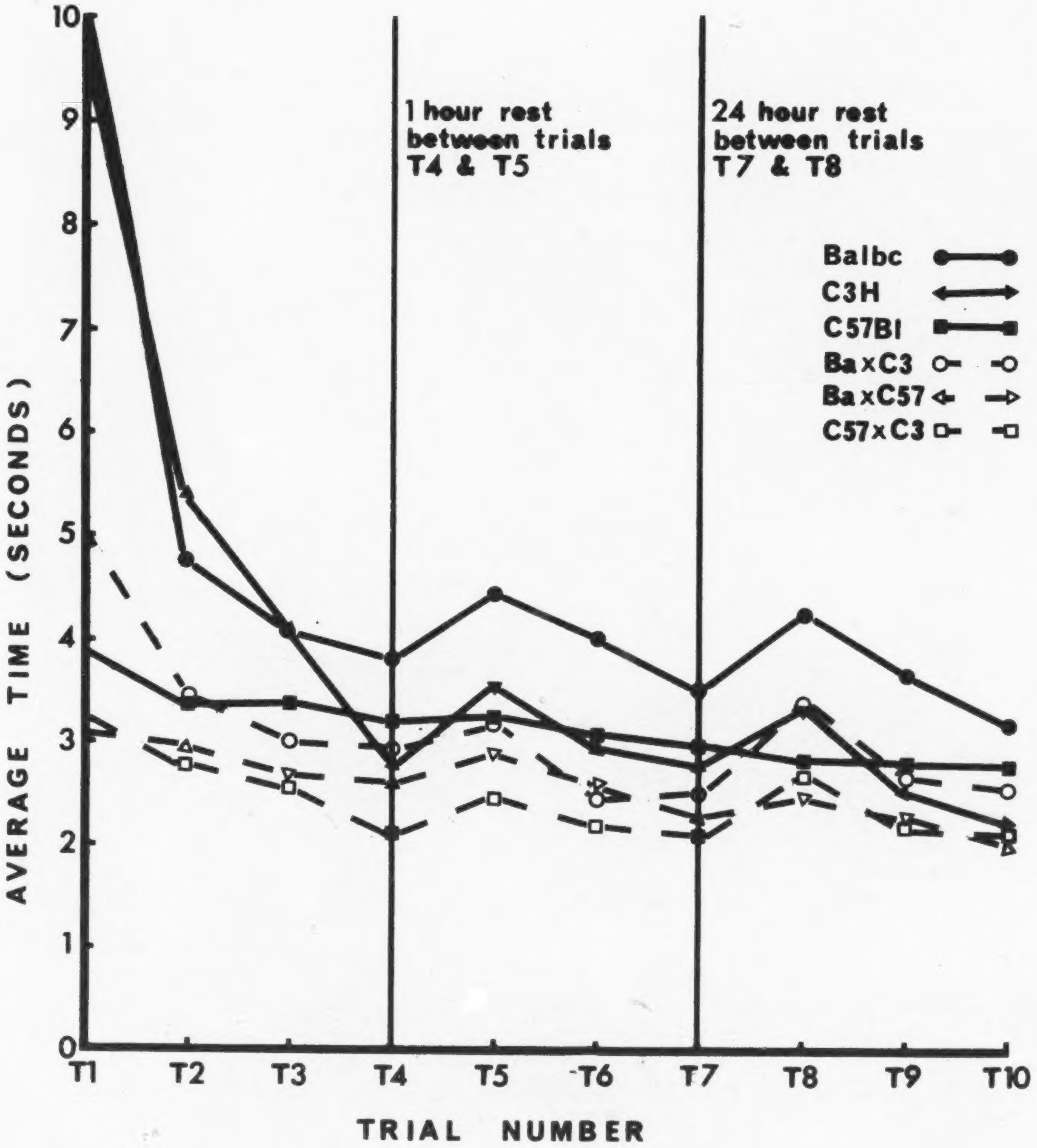
	B	C	D	E
A	0.032	0.200	0.143	-0.216
B		0.081	0.039	-0.095
C			-0.074	0.125
D				-0.121

TABLE 5

Percentage of "no shock jumps" for trials 2 to 10
(male data only) - after Rose and Parsons (1970).

	Ba	C3H	C57	Ba x C3H	Ba x C57	C3H x C57
T2	-	-	-	-	-	1.3
T3	0.7	14.8	-	3.1	2.2	9.3
T4	2.8	22.2	2.0	10.2	9.6	22.7
T5	1.4	16.0	1.0	2.0	7.4	12.0
T6	0.7	20.0	3.2	19.4	14.8	17.3
T7	3.6	20.0	7.4	20.4	29.6	32.0
T8	1.6	4.5	6.9	12.7	18.9	12.0
T9	4.0	13.6	9.7	11.4	23.6	24.0
T10	9.5	31.8	12.5	16.5	37.8	29.3
Total	2.6	15.8	4.3	10.4	15.8	17.8

Fig. 1 Average time in seconds for each of the 10 successive trials for the three inbred strains and hybrids. Male data only are given, but the female data were similar (after Rose and Parsons, 1970).


1 hour rest between trials T4 & T5
24 hour rest between trials T7 & T8
Balbc
C3H
C57Bl
BaxC3
BaxC57
C57xC3
AVERAGE TIME (SECONDS)
0
1
2
3
4
5
6
7
8
9
10
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
TRIAL NUMBER

QUALITATIVE ASPECTS OF GENETICS AND ENVIRONMENT IN THE DETERMINATION OF BEHAVIOR

by

Claudine Petit

Paper Prepared for C.O.B.R.E. Research Workshop on
GENETIC ENDOWMENT AND ENVIRONMENT IN THE DETERMINATION OF BEHAVIOR
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QUALITATIVE ASPECTS OF GENETICS AND ENVIRONMENT IN THE DETERMINATION OF BEHAVIOUR .

by Claudine PETIT[*]

The quarrel between "innate" and "acquired" has been going on for years and yea It has at last been settled in the morphological and physiological field thanks to the progress of Genetics; this science has demonstrated that genes act according to a process which varies with the conditions in which these genes regulate the syntheses, so that the phenotype results from the interactio between genotype and environment. But opinions still disagree strongly when it comes to behaviour, for here the importance of learning makes the genetic analysis particularly complicated..

I, as a Geneticist, think that it is a false problem; everything, at bottom, is a matter of Genetics; whatever it may be, either the weight of a cow, the performance of a racehorse, or the sexual advantage of a Drosophila, the extreme limits of the characters are genetically determined. Of course, non-genetic factors such as the composition of the inner medium, and the physical or biological environment, may intervene on the genetic basis . If these are applied at the proper time of life of an individual, including its embryonic development and growth, they can bring about a deep change in the manifestation of the character. Hence the great difficulty of this type of study, where the variabilit due to the impact with environment must be added to the genetic variability, quite considerable in itself, that normally exists in any population.

Genetic variability alone reaches the minimum value of 40% of heterozygous, as shown by the works of DOBZHANSKY and his collaborators on genetic load (DOBZHANSKY, I957) and that of LEWONTIN on enzymatic polymorphism (LEWONTIN and HUBBY, I966). Analysis of results generally requires the use of complex mathematics and experiments must be carried out on a large number of individuals in order to distinguish the true results from those of individual variability.

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The question is not only to evaluate the genotype-environment interaction, but the genotypes-environment interaction, without knowing how many genotypes are involved. The nature-nurture relation reaches here its utmost complexity, as different and badly known genotypes interfere with environment, so that the undertaking of any mathematical or experimental analysis is very complicated.

Mankind, whose behaviour is submitted to all types of environments, inner medium, and both physical and biological environment, might appear to be the best species for such a study, especially as a sound knowledge of these interactions would be important for education. But culture has to be added to the three other environments, si tightly intertwined that they can only be separated by experimentation. Furthermore, how can the most serious scientist be expected to keep a cool head when dealing with his awn kin ? Lastly,the number of human genes is very high. For all these reasons endless difficulties arise when one endeavours to tackle the problem in mankind.

I have been set with the task of studying the : "Qualitative aspects of Genetics and environment in the determination of behaviour." This subject covers nearly all Behavioural Science, so I will only give its great outlines and base my arguments on some well analyzed examples. Three points will be considered in turn :

- genetic determination of some behaviours and the influence of physical environment on genotype,
- influence of biological factors ans inner medium on gene action,
- influence of biological and social environment : imprinting, conditioning, learning and the advantage of the rare type. Badly known up till now this phenomenom may play an important part in evolution.

GENETIC DETERMINISM AND THE INFLUENCE OF PHYSICAL ENVIRONMENT ON SOME BEHAVIOURS.

Behaviour is determined by responses on the organism to external signals. These signals are sent out by alien or conspecific individuals, by objects or physical phenomenons; they generally release simple behaviours of attraction or flight. They are perceived by sensorial receptors and integrated by the central nervous system. Deficiencies at either level perturb behaviour.

The cases that the easiest to analyze are naturally the mendelian gene dependent behaviours, especially when they are independent of environment or released by very precise environments. These behaviours are nearly always due to a faulty metabolism : first MAYER and al. (I95I), then FULLER and JACOBY (I955) have thus observed that these recessive gene responsible for obesity in some strains of mice leads the homozygous to select fat food. In the same way, schizophrenic behaviour, probably owing to a metabolic error that troubles perception (HUXLEY and al , I964), is determined very often by a single partially dominant gene, of low penetrance (SLATER, I958); Circling and choering behaviour, well known in mammals and birds are the result of nervous system injuries caused by mendelian genes lethal in the homozygous state. In mice, audiogenous crises are determined by a recessive gene (LEHMAN and BOESIGER, I964). Abnormal behaviours, as result of mendelian genes are also found in Drosophila. The Hyperkinetic genes (Hk^{Ip} or Hk^{2P}) produce a leg-shaking action, in response to ether vapour (KAPLAN and al,I97I).

It is curious to note that on the contrary, apparently simple behaviours such as taxis have a polygenic determinism. The difference may come from the fact that the abnormal behaviours are pathological, and do not correspond to any organized pattern, while taxis have a serious adaptative value for the species and require precise sensilla and a good central nervous integration. Such complex and different elements have only very few chances to be controlled by a single gene.

Phototaxis was studied in *Drosophila melanogaster* by HIRSCH and TROYON (I956) and in *Drosophila pseudoobscura* by SPASSKY and DOBZHANSKY (I967). A multiple choice apparatus allowed the selection of positive or negative phototaxis in inbred or heterogeneous strains. The responses showed polygenic determinism.

Geotaxis was studied in the same species using the same technique. The results were identical and led to the selection of strains with a positive or negative geotaxis (HIRSCH and BOUDREAU, I958; EHRMAN and al,I965).MEDIONI (I96I),on his own, showed different orientations in strains of *Drosophila melanogaster* of different geographic origins. ERLENMEYER-KIMLING and HIRSCH (I96I), working on marked chromosomes, made strains homozygous for some particular chromosomes; they demonstrated that genes of the X chromosome control positive geotaxis, and genes of the 3 rd chromosome negative geotaxis. In another strain, chromosome 2 was proved to bear factors causing positive geotaxis. So, the three chromosomes are responsible for this behaviour.

But these taxis are not independent of environment. The experiments just mentioned were carried out at a set temperature with controlled moisture and lighting, and their results only apply to these special conditions. Naturally environment is abble to change phototaxis. THe beetle *Blastophagus pinniperda* L. is positively phototactic in spring, at temperatures between I0° and 35°C, but negatively phototactic below and above this temperature (PERTTUNEN,I958, I959). In the fall, the range is reduced to 20°-30°C. THus a temperature of I5° induces positive phototaxis in spring, buy negative in autumn, when the animal starts looking for winter hides. In the weevil,*Calandra granaria* , where genetic changes of the phototaxis where shown by selection (RICHARDS, I95I; PERTTUNEN,I963) found phototaxis more and more positive as the dryness increased. Such a change in a behaviour, the selective value of which is evident, may easily be explained by the influence of physiological factors on the way of the genes act.

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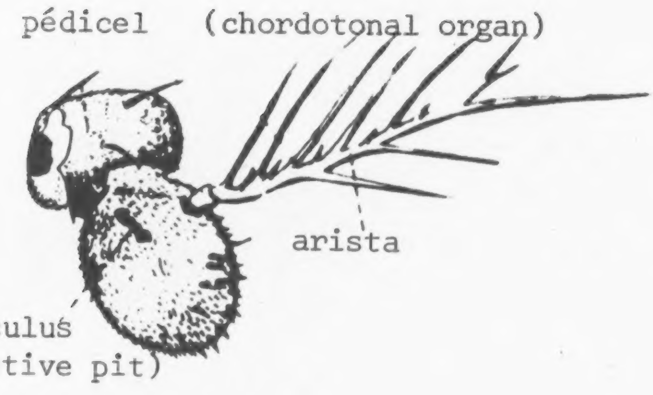

pédicel
(chordotonal organ)
arista
funiculus
(olfactive pit)

Fig.1 - Drosophila melanogaster: the antenna.

The importance of sexual behaviours was discovered by DARWIN (I87I), and is now generally accepted. These behaviours have been submitted to many investigations for the last thirty years. THey lead to speciation and they play a prominent part in the maintenance of genetic variability among populations. They are very complex behaviours, as they are the result of a chain of stimuli and responses between the male and the female. THey were studied in a variety of species, mice , guinea-pigs, the fisch Platypoecilus, and especially Drosophila, whose different species provide a tremendous amount of genetic behavioural and sensorial informations.The description of the courtshi of Drosophila melanogaster by BASTOCK (I956) is classical and may be used as a basis to study any courtship of Drosophila. The courtship takes place in THree phases :

-orientation, during which the male stays behind the female, or follows her if she starts walking,

-vibration, that corresponds to a great period of agitation in the male; the fly with an horizontally kept wing, vibrates and circles the female, keaping his head always turned towards her,

-licking immediately precedes mating; during this phase, the male prods the abdomen of the female with his proboscis, just before he makes an attempt at copulation.

It seems clear that the first phase corresponds essentially to olfactive or visual stimulations, the second, to auditive and tactile stimulations, and the third to tactile and chemical stimulations. Ablations of affectors or receptors have made it possible to define the importance of these different kinds of stimuli. The importance of the antennae as receptors of the stimuli during courtship was first shown by MAYR (I950): antenneless females of Drosophila pseudoobscura or Drosophila persimilis proved less discriminative in front of the males of the foreighn species than the normal females. Later on, the precise ro role of the different parts of the antennae was defined by PETIT(I958,I959) and MANNING (I967).

The antenna includes three segments (fig.I) : scape, pedicelle with Johnston's organ that responds to vibrations and funiculus with olfactive pit and arista. So it was thought that the ablation of the different parts might give some informations; though manú different sensilla cover the body of the fly, the results were clear enough. The ablations were made during the narcosis necessary for sexing; the virgin were left to grow older in a unisex group and two days later, males and females were put together, without anesthesia, for 24 hours. The percentages were compared either with those of normal flies for the aristaectomized flies, or with those of injured flies for the antennectomized ones. The results show (PETIT,I958), that the ablation is more harmful for the female than for the male : 54 % of the antenneless males fertilize females while only 8% of antenneless females are inseminated. This implies that the receptors of the females must be essentially on the antennae, while those of the male are scattered all over the body. This conclusion is in good accordance with the direct observation of courtship during which the male keeps touching the female with his legs and proboscis. It allows to suppose that the stimuli received by the male are essentially chemical and tactile, and those received by the female, auditive and perhaps olfactive. The aristaectomie is only slightly harmful for the males (74% of inseminations against 88% in the controls), but it is very prejudicial to the females; their percentage of mating falls to 43%. The explanation of the role of the aristae was given by MANNING (I967) : a thin glass needle was stuck on to the aristae of the females, to prevent them from vibrating; the percentage of mating fell dramatically. This is because they are used in correlation with the chordonatal organ to amplify the vibrations. An olfactive stimulation of the female may exist in this species, as the destruction of the funiculus with its olfactive pit lowers the percentage of mating to 30%. Still, as the injury is very different and the comparison of the percentages by the t test only slightly significant, this result is not sure. In Drosophila melanogaster, vibration thus appears to be an important stimulus for the female, while the male responds to tactile and olfactive stimuli.

Such complex stimuli are liable to be sensitive to environment. THeir analysis in many groups shows the influence of genotype and environment, physiological medium as well as physical and biological environment, with learning and interactions between individuals in some cases. The genetic analysis was carried out mostly in Drosophila, as the formal genetics of the genus are well known and allow to handle the chromosomes with great precision. The influence of physical and biological medium was examined, not only in this group, but in Vertebrates, especially in the case of biological environment, and particularly so in birds and mammals.

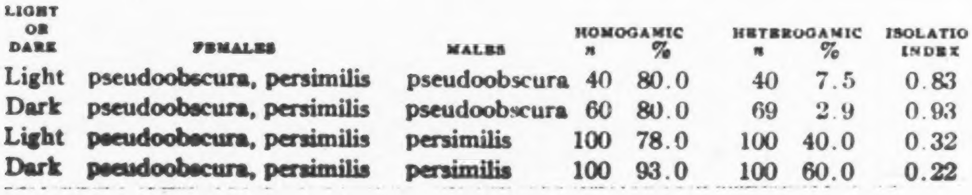
In Drosophila, a sexual selection was demonstrated between geographical races, or simply between strains of different geographical origins, when searching for incipient isolations : DOBZHANSKY and STREISINGER (I944) show a north to south gradiant in the vigor of *Drosophila prosaltans* males. MAYR and DOBZHANSKY (I945) describe selective matings between strains of different geographical origins in *Drosophila pseudoobscura* and *Drosophila persimilis*. Incipient isolations appear in some cases as in *Drosophila arizonensis* and *mojavensis* (BAKER,I947) or *Drosophila sturtevanti* (DOBZHANSKY,I944). A similar result was found when studying sexual selection between strains differing by inversions.BRNCIC and KOREF-SANTIBANEZ (I964) worked on *Drosophila pavani* and *Drosophila gaucho*, SPIESS and his collaborators on *Drosophila persimili* (SPIESS, I962; SPIESS and LANGER,I964 a and b; SPIESS and al, I966; SPIESS and SPIESS, I967), DOBZHANSKY and his collaborators on a wide variety of species especially *Drosophila pseudoobscura* and *paulistorum* (for a review, see PETIT and EHRMAN,I970).

All these results are in favour of a polygenic determinism. However, some authors(reviewed by SPIESS, I970) describe a sexual selection between strains that differ only-theoretically- by one gene : PETIT(I95I,I954) demonstrated sexual selection between strains that differ only by the *Bar* or *white* gene in *Drosophila melanogaster*. BASTOCK (I956) studied the competition between *yellow* and *wild* and demonstrated that the *yellow* male was at a disadvantage with *wild* females.ELENS (I957) came upon the same results with *ebony*, and in some cases, thought them to be caused by a cytoplasmic factor.

The existence in Drosophila of marked chromosomes, used for making homozygous strains for chromosomes, allowed to choose between the two hypotheses. In the experiments involving Bar and white, sexual selection might appear as a pleiotropic effect of the gene; but the transferring of these genes in other genetic backgrounds changes the intensity of sexual selection; and so it was proved that it depends on an interaction between the genes Bar or white and the genetic background (PETIT,I958). Selection experiments led to the same conclusion: with a polygenic determinism, the selection of any character produces a change in the genetic background, and, as a consaquence, a change in the sexual selection or isolation; this result was found by MATHER and HARRISON (I946), when selecting flies for greater and smaller numbers of chaeta on the abdomenal sternites in Drosophila melanogaster. It was also found by del SOLAR (I966) and by EHRAMN (EHRMAN and al, I965) when measuring sexual selection between strains selected for positive or negative geotaxis or phototaxis.

THis polygenic determinism, at first obvious when one thinks of the complexity of courtship, was partially explained by EWING (I969,I970). In a precise acoustic study of the courtship songs of Drosophila, he demonstrates that the genes which control the song patterns are located on the X chromosome, while quantitative features are controlled by autosomal genes. TAN (I946 found similar results in Drosophila persimilis, where sexual isolation is changed when the X and 2^d chromosomes are modified. This study is all the more interesting as it is directed at one of the main stimuli of courtship and opens the way to a precise genetic analysis of a behaviour.

It can now be thought that all the components of physical environment that act on vibration change the sexual selection intensity. REED, WILLIAMS and CHADWICK (I942) demonstrated a positive correlation between the mean frequency of vibration and temperature in four different species of Drosophila.Moreover, the vibration frequency is in correlation with the ratio of the volume of



LIGHT OR DARK	FEMALES	MALES	HOMOGAMIC		HETEROGAMIC		ISOLATIO INDEX
			n	%	n	%	
Light	pseudoobscura, persimilis	pseudoobscura	40	80.0	40	7.5	0.83
Dark	pseudoobscura, persimilis	pseudoobscura	60	80.0	69	2.9	0.93
Light	pseudoobscura, persimilis	persimilis	100	78.0	100	40.0	0.32
Dark	pseudoobscura, persimilis	persimilis	100	93.0	100	60.0	0.22

Table I - Mate discrimination in the light and in the dark (from Mayr and Dobzhansky, I945).

flight muscles and wing size. Temperature does influence sexual selection and isolation. However, one must not conclude that it is surely and only trough vibration that temperature exerts its influence, because temperature changes the rate of development and, as a consequence, size and the delay of maturatio MAYR and DOBZHANSKY (I945) demonstrated that the isolation between *Drosophila pseudoobscura* and *Drosophila persimilis* is lower at I6° than at 25°C, the persimilis males being the most sensitive (table I). The intensity of the selection between white and wild varies with the temperature. The differences in mating speed found by PARSONS and KAUL (I966) and SPIESS, LANGER and SPIESS (I966) with AR and PP karyotypes of *Drosophila pseudoobscura* are probably due to this factor. The vigor of the two karyotypes is the same when they are kept at I5°C. But when they are kept at 25°C, the mating speed of PP suddenly increases. Similar results are found for *Drosophila persimilis* (SPIESS,I970); as WT and KL have not the same optimal temperature, WT mates quicker when the temperature is low, and KL when it is high. In any case, heterosis is higher for limit than for optimal temperatures; and this is not only true for sexual behaviour, but for the all components of fitness (DOBZHANSKY and LEVENE,I955); it appears as one of the aspects of genetic homeostasis.

Moisture probably changes sexual selection, as I myself have seen, but this question has not to my knowledge been the object of any systematic research. It is all the more likely so as the optimum of dampness varies from one specie to another and moisture may change the taxis in some species (cf. P. 4).

Light is important too. Species abble to mate in the dark are slowed down in complete darkness (SPIETH,I952, SPIESS and HSU,I950). Some species, such as *Drosophila subobscura* are unable to mate in the dark. The total amount of copulations is changed by light in *Drosophila prosaltans* (MAYR and DOBZHANSKY, I945) (Table I). In *Drosophila pseudoobscura*, there is a negative correlation between mating ability and light intensity (ELENS and WATTIAUX,I970).

In *Drosophila melanogaster*, some mutants such as *ebony* are sensitive to light (RENDEL, I95I). The *ebony* males, that are at a disadvantage in competition with wild males in the light, are, on the contrary, at an advantage in the dark. A complete study of the relative importance of vibration and light was made by GROSSFIELD(I966,I968).

It is evident that this influence of environment on sexual selection or isolation must imply important evolutive consequences. Some species, slightly isolated when the temperature is low are nearly completely isolated when it is high. So either a spreading of the territory belonging to the two populations to warmer countries, or a change in the climate are able to create an isolation between strains that showed none. Morever, the alternance of the advantage between two forms according to the environment may be a way of maintenance of polymorphism, the adaptative advantage of which has no more to be demonstrated. And one can but follow Barker's warning (1967) when he writes that the evaluation of sexual isolation in a precise experimental design does not allow to conclude that the isolation exists in nature.

INFLUENCE OF PHYSIOLOGICAL FACTORS AND HORMONES ON GENES

Other environmental factors are able to change behaviour through physiological factors and via blood.

Physiological factors depending on rearing conditions, age or composition of blood are well known in the determination of some behaviours[1], especially that of sexual behaviour. In Drosophila, the components of sexual behaviour are behavioural and metabolic factors (FAUGERES,PETIT, THIBOUT, I97I), such as athletic ability of Smith, or male vigor, evaluated as the ability of heterozygous males to inseminate more females than the homozygous do (BOESIGER,I958, I962). There are moreover factors of learning, but I shall devote my attention to those later. And so, it is not surprising that the rearing conditions have an important influence on sexual activity and that flies reared in overcrowded conditions are at a disadvantage when competing with over-fed flies (PETIT, I958;ROBERTSON,I963;KAUL and PARSONS,I965; SPIESS and SPIESS,I969). Lack of yeast during larval growth and adult maturation delays mating and lowers receptivity in females (MANNING,I967;SPIESS and SPIESS,I968).

Age is another factor that influences sexual activity. All Drosophilists know that sexual maturity does not appear at the same age in the different species, even when the rearing conditions are the same. Besides, sexual activity can change during the course of life : in *Drosophila melanogaster*, one can see that *wild* flies mature very quickly, but their activity remains constant; on the contrary, the activity of *white* males develops more slowly, but becomes as good as and even better than that of *wild* (PETIT,I958). The same thing happens in *Drosophila persimilis*; KL and MD karyotypes have the same speed of mating when the temperature is low, this speed increases for five or six days in MD, then declines, while that of KL is maintened (SPIESS,I970). This change is very likely due to hormonal influence. Sexual receptivity in *Drosophila melanogaster* appears on the second day after batching; it corresponds to an increase of *corpora allata* that secrete the juvenile hormone (DOANE,I970).

The hormonal influence was proved by injections of the complex contained by corpora allata given to pupa I7 or I9 hours before batching. The controls received only a bit of the aorta. The injected flies were receptive on the first day; control and normal flies were receptive on the second day (MANNING, I966).

However, Invertebrates are not good material for this kind of research, and more precise informations are given by Vertebrates. The effect of hormones on behaviour, and especially that of steroïds, oestrogens and testosterone on the sexual behaviour of Mammals and Birds has been known for a long time. It is still necessary to precise the nature of interactions that induce hormones to change the genetically determined behaviour patterns. The problem is difficult because of the interference of social experience that interferes with the preceding factor. But I will not deal with this subject just yet.

A fairly complete study of sexual behaviour of the guinea pig was made, viewing it from the different angles of behaviour. VALENSTEIN,RISS and YOUNG (I964) looked at the behaviour of the males in two inbred and one heterezygous strain. In one of the inbred lines, the amount of preliminary courtship behaviour was stronger than in the other, whereas the other strain had higher frequencies of behaviour in the categories related to actual impregnation. But both had a sexual drive lower than that of the heterozygous stock. The same kind of difference was proved to exist in females (GOY and JAKWAY,I959). From these results, the genetical origin of the differences was ensured. At the same time, GRUNT and YOUNG (I952,I953) investigated on the action of hormones. THey distinguished in their male guinea pigs three levels of sexual behaviour,high medium and low, and castrated the three stocks. After the castration, all animals had a low sexual drive. Sixteen weeks later, the castrated guinea pigs were injected with testosterone propionate; their sexual behaviour reappeared. Still, though the three stocks received the same amount of hormone, the levels of sexual activity were different, and identical to those of their category before the castration. The same results were found in females by GOY and YOUNG (I957). This result proves that the differences in sexual behaviour are not the result of different amounts of hormone, but are due to different responses to sexual hormones of the tissues responsible for sexual behaviour. And these responses are genetically determined.

Another problem is to know how hormones act on the gene. The gene-environment report will probably deal with this subject, so I will only throw a quick glance at it.

The gene ensures the synthesis of proteines, the sequence of the DNA nucleo tides controls the nature and the order of the aminoacids of the protein controlled by this gene. The transcription is done thanks to different RNA. It has now been shown that a wide variety of hormones can affect gene activity this conclusion is strongly supported by the fact that each of these hormones is powerless to exert some or all of its characteristic effects when the genes of the cell on which it acts are prevented from functioning. For oestrogenes, a genic regulation was shown : in castrated females injected with oestrogenes, the protein synthesis of the uterus are multiplied by 3. It is the same for male hormones; they activate the gene. and injection of testosterone propionate induces a tremendous increase of the RNA synthesis in the different cells So,the action of genes can be modified by different physiological factors, during or after the development.

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INFLUENCE OF BIOLOGICAL AND SOCIAL ENVIRONMENT

The influence of biological and social environment must be added to the action of physical and internal environment. This influence differ greatly, according to the psychic level of the species under study. It includes phenomena such as imprinting, learning or the advantage of the rare type. Here, one comes up against the problem of innate and acquired, that bitterly divided and divides even to-day the psychologist and the sosiologist. A look at the problem of learning is of primary importance for man, but it is too often examined with philosophical a priori, all the more difficult to discard when cultural environment is superimposed upon biological environment. Everyone bears in mind the theory of the I8 th century philosophers : man is good when he comes into the world and is only spoiled by a bad education.

It is not for me to examine the ultimate aspect of education. I shall devote my attention to animal experimentation, in hopes that some models may be applied to the human species.

One of the most remarkable aspects of the influence of the environment in the determination of behaviour is imprinting.Imprinting is concerned with the first social ties in young animals; these early ties have an important influence on the social behaviour of the adult. Thus,ducklings follow the first moving thing that they catch sight of when they are born; and if this object is not their mother, they stay as tightly bound to it as they would their mother As adults,, their social behaviour can then be perturbed; they may court this object, instead of animals of their own species. In I909, CRAIG observed that two species of wild pigeons could mate when the young of one species were brought up by the parents of the other species. These youngs,as adults, preferred the birds of their foster parents species. HEINROTH (I9I0;I924,I933) ascertained the same kind of behavion in several species of European birds. LORENZ (I935) studies it in the graylag goose.

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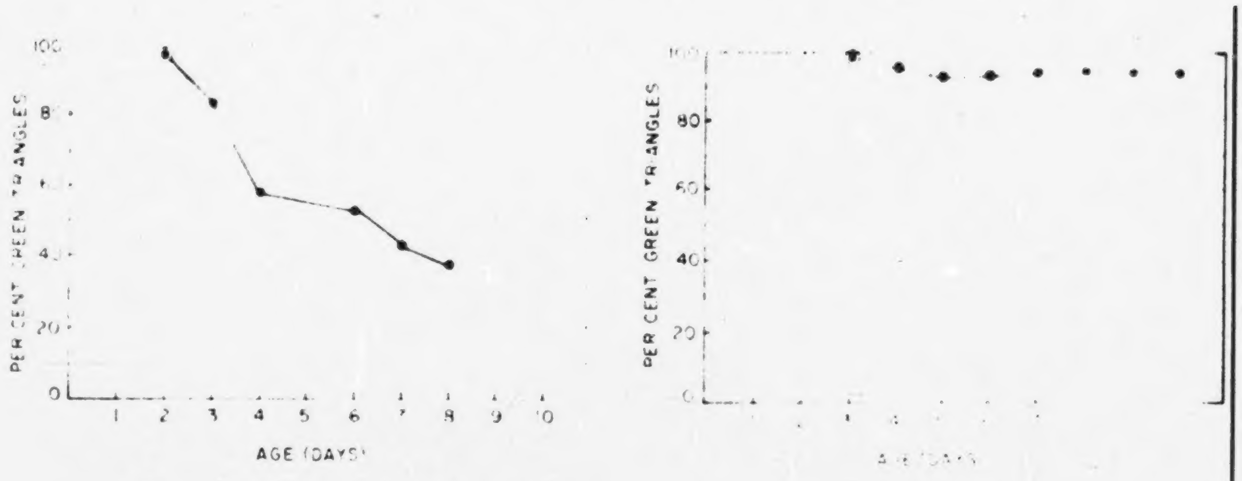


Per cent of responses made to green-triangle by chicks given the reinforcement experience at the age of 2 days, in terms of cumulative total per cent of responses

Cumulative total per cen[illegible] made to green-triangle during [illegible] by chicks given the reinforcement [illegible] age of 3 days

Fig.2- Reenforcement is possible during a specific and short period (from Hess, Roots of behavior).

These phenomena only occur during a precise stage of development. This is clearly proved by Hess'experiments on chicks (I962). Chicks usually peck on preferential spots. Thus, when Leghorn chicks have to choose between white circles on a blue board and white triangle on a green board, they prefer the blue board with the circle; on the contrary, Vautress Broiler chicks prefer yellow to another colour. THis innate behaviour can be changed by the establishment of conditionned reflexes, if the experiment is performed at a particular time. If one adds a hole with seeds inside the spot, the chick changes its behaviour and pecks on holes with seeds, even if the stimulus is not comprised of the innate colour. When the seeds are taken away, this preference is kept up for a while. Experiments made with chicks of different ages show that renforcement is only possible for a very short period : one-day old Leghorn chicks renforced for green, instead of being left to their natural preference for blue, return to innate behaviour patterns as soon as the stimulus is removed. In two days old chicks, the preference for green reduces quickly, however in three day old chicks it is permanent, while in older chickens, it disappears with the stimulus. Thus a critical period exists at the age of three days.

Too little is known about developmental genetics and the nature and genetic determination of these phenomena, to allow a genetic interpretation. But they call to mind some well known facts in morphological genetics : the Bar mutatio in Drosophila melanogaster reduces the number of ommatidia, and the reduction increases in importance as temperature rises but this action is only possible during a short period of development (CHEVAIS ,I943). This means that environment can only change the action of genes at a given time of development.

The influence of social environment on normal sexual integration during the first hours of life is a similar problem, as shown by the work of VALENSTEIN, RISS and YOUNG on the guinea pig (I955). Besides the genetic and hormonal factors, they look at the social components in the determination of this behaviour. The males of two inbred strains and one heterozygous strain were reared either together, or isolated. They were all separated from their mother at 25 days of age. At 77 days of age, males were presented to females in oestrus and different parameters were recorded, the most important being the number of ejaculations. The results are as follows :

	isolated	controls
line 2 (inbred)	6%	84%
line I3 (inbred)	8%	57%
heterozygous line	7I%	I00%

In the two inbred lines, the sexual performances of the animals reared together were better than those of the animals reared separately. As there was only a slight difference in performance in the heterozygous line, the authors thought that the 25 days old animals might have been socialized earlier due to a faster rate of development. To test this hypothesis, they separated the heterozygous guinea-pigs from their mother at I0 days of age. Under these conditions, the sexual behaviour of the isolated males was not as good as that of the males reared together.

A similar phenomenon was described in an animal with a more elementary psychism Drosophila . MAYR and DOBZHANSKY (I945) reared males of Drosophila pseudoobscura and Drosophila persimilis with either females of the same species or with alien females; they then let them choose between the two kinds of females. Although no difference appeared in Drosophila-pseudoobscura, in persimilis males reared with females on the same species discriminated more against alien females than males reared with pseudoobscura females. MAINARDI (I968) observed similar results with Drosophila melanogaster. Males of a wild strain were divided as soon as they hatched into 3 groups. The first were grown under normal conditions, with wild females, the second with yellow females, and the third in isolation. The males were then given a choice between yellow and wild females. Males reared normally courted the wild females first; while on the contrary, males of the second and t the third groups mated at random.

It is clear that fixation is genetically determined, but the result of gene action depends up on environment and may be considered to be phenotypic. In nature, the young animal is reared by its parents; imprinting which occurs at a precise stage in the course of development (HESS,I959,I962), ensures the integration of the individual in its social group and provides sexual isolation that is good for the species, by maintenaing coadapted genes together.

Another aspect of behaviour, half-imprinting, half-learning with genetic and environmental aspects, is represented by the songs of birds. The chaffinch is especially interesting from this point of view with the basic pattern song being innate all of the finer details and much of pitch and rythm being acquired by learning (THORPE, I954,I958 a and b). A good analysis of song is now possible. The normal song, territorial proclamation and stimulation for the female, consists of 3 phrases :

- Phrase I has from I to 4 notes, usually somewhat crescendo and normally with a gradual or step-wise decrease of mean frequency;
- Phrase 2, generally distinct, but not always, is made by a series of 2 to 8 notes, of constant frequency, lower that that of phrase I;
- The song concludes with phrase 3, consisting of I to 5 notes, with a more or less terminal flourish.

In a first series of experiments, birds normally reared by their parents were separated from them in September, in order to study their song the next spring. If the young were exposed to all bird songs during development-that of chaffinch and other species- their song was normal. If the young were exposed tc no other birds but their companions from September to May, the result was different : phrase I and 2 were normal,but phrase 3-specific to each community c of young birds- was slightly abnormal. In a last series of experiments, the

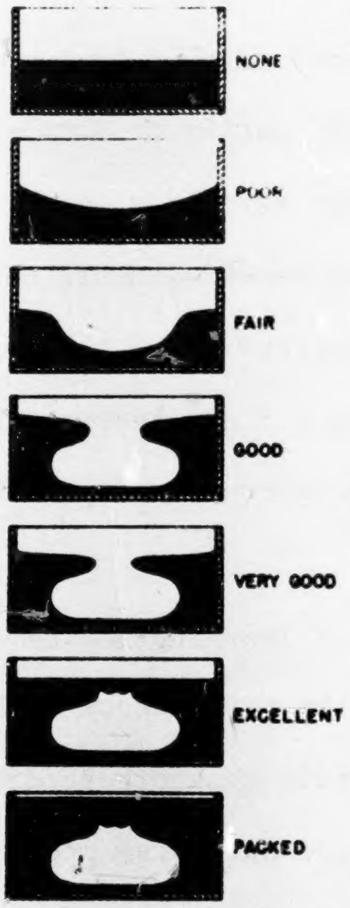
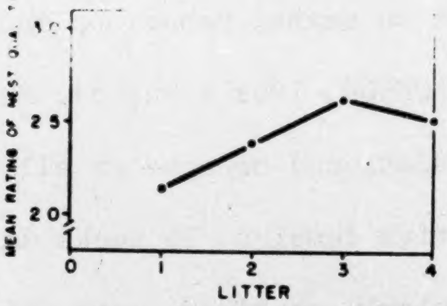

NONE
POOR
FAIR
GOOD
VERY GOOD
EXCELLENT
PACKED

Illustration of a graded series of maternal nests built by the pregnant rabbit. The various types of nest observed grade from no nest at all to a hollowed-out and closed-over nest well packed with hair plucked from the body and nesting material. (From Sawin and Crary, 1953)



Mean nest-quality score for the first four litters of 84 females. (From Ross et al., 1956)

Fig.3 - Maternal behavior and experience in the rabbit.

birds were hand-reared and never allowed to hear an adult song; phrase I and 2 were correct, but phrase 3 was partly or completely lacking. Each community had an entirely individual, but extremely uniform, community pattern.

It seems here that some modulated elements can be added to innate song which is considered to be a fixed expression of the genes expressed in phrases I and 2 The modulated elements of phrase 3 are learnt during the social phase that follows birth; they can be considered as a phenotypic manifestation, developped perhaps by sexual selection.

A somewhat different kind of learning may develop from repetition of the same situation, for instance the perchase of maternal behaviour in rabbits. Differences exist from one strain to another; differences in nest-building, nesting time, plucked haire, and agressive protection of the young prove that these activities are genetically determined (SAWIN and CURRAN,I952).Nest-building and plucked hair were specially studied (SAWIN and CRARY, I953). Nest-building is not an all or nothing process and a lot of intermediaries exist between the absence of nest and the perfect nest (fig.2). Observation of the quality of nests during the first 4 parturitions of 84 females demonstrated an improvement during the first 3 litters; after that no further progress was registered (fig.3). This seems to be result of experience, but as the author suggests, unknown physiological changes cannot be excluded.

Experiments of another sort on sexual behaviour and experience have been made on the cat (ROSENBLATT and ARONSON, I958 a and b). Male cats, with sexual experience (from 32 to 8I copulations) or none at all were castrated. They were then tested weekly with receptive females. I5 weeks later, sexually experienced males, whose sexual activity slowly declined, were still greatly superior to non experienced males. When the animal was castrated before sexual maturity, sexual behaviour never developed. This proves that genetically determined sexual behaviour, released by hormones and developped by experience,persists even after the hormones have disappeared.

19hrs

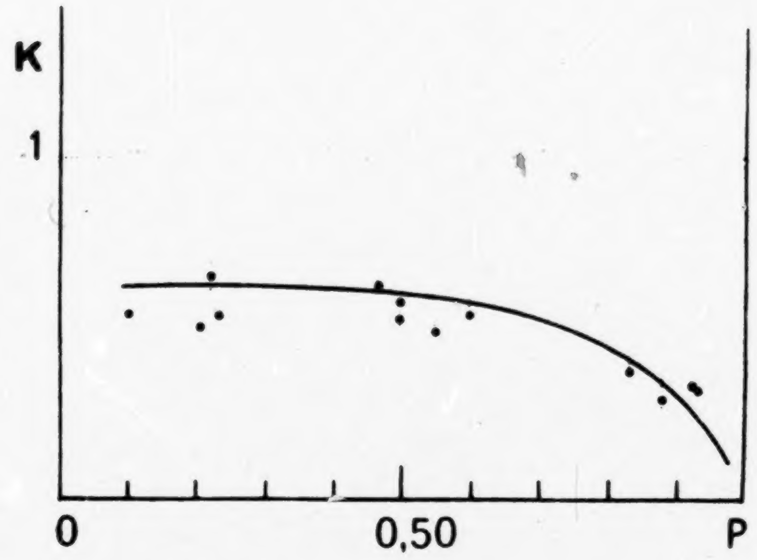


Fig. 4 a

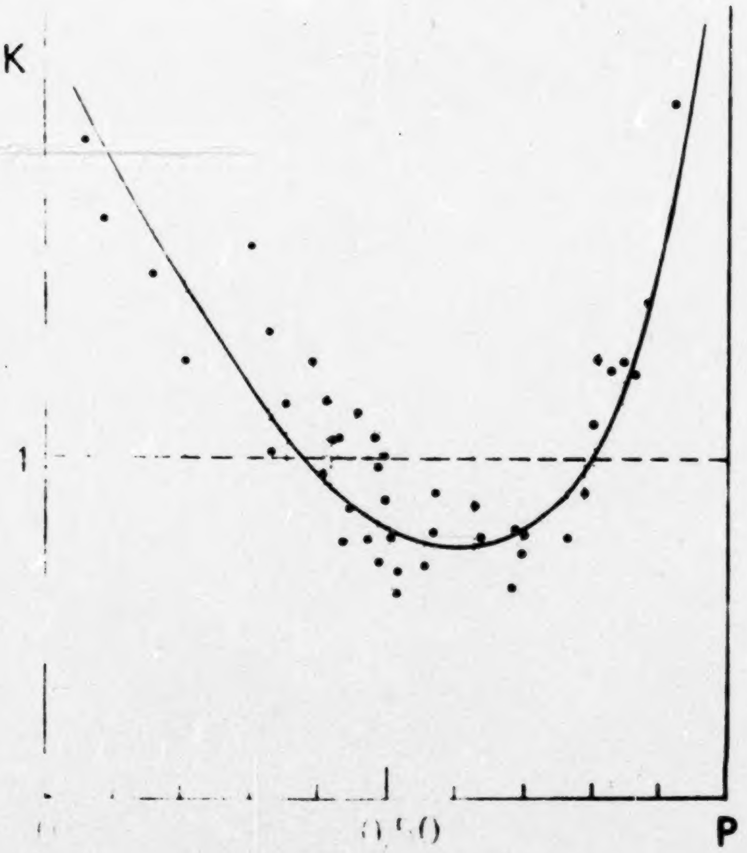


Fig. 4 b

Fig.4- Frequency-dependent selection in Drosophila melanogaster.

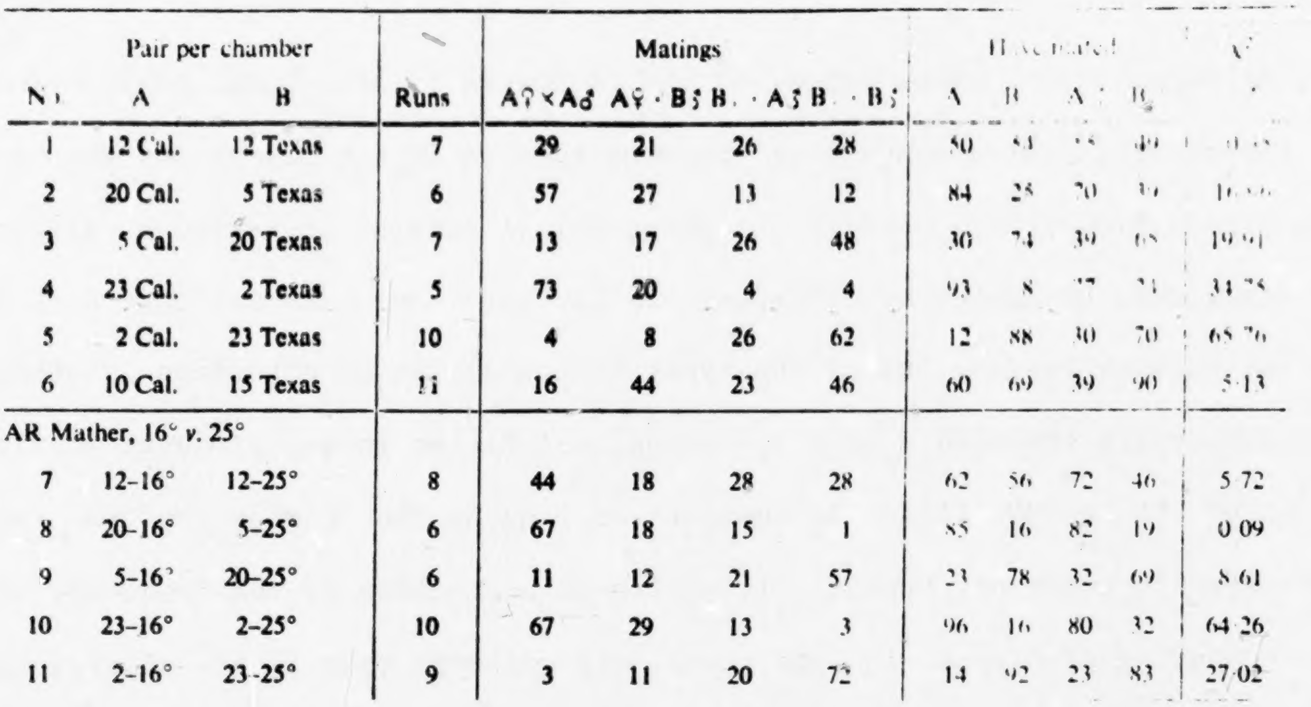
4 a) Sexual selection between Bar and wild

4 b) Sexual selection between white and wild (from Petit, I95I,I954).

An especially curious aspect of the influence of biological environment on behaviour is the advantage of the rare type in sexual selection. When male and female Drosophila of different geographical origin, or reared at different t temperatures, or marked by different visible mutations, are put together, they do not mate at random. One of the types is usually at an advantage in either sexe,generally the male . This advantage, calculated in experimental populations of 200 to 2000 flies, is constant as long as the frequency of the two genotypes is constant. However, it varies as a function of the frequency of the two competing genotypes. In some cases, the genotype that is at a disadvantage when it is abundant in the population, is at an advantage when it becomes rare.

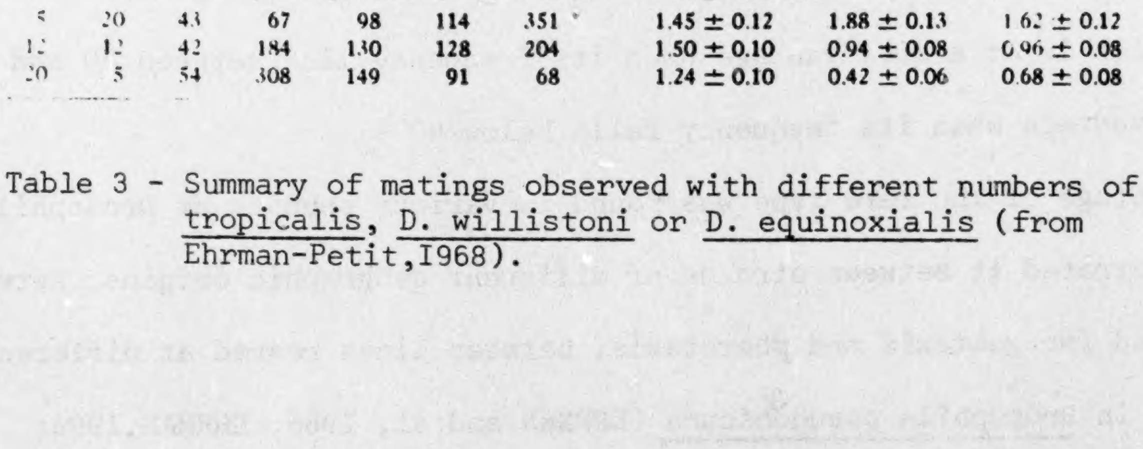
Frequency-dependency was discovered in *Drosophila melanogaster* (PETIT,I95I) when competition between *Bar* and its *wild* allele was studied. The advantage of the rare type was clearly demonstrated with the white mutant (PETIT,I954). In these twO cases, selection occured between the males, and the female genotype had no influence. A coefficient of mating success and a relative selective value were calculated. If *p* and *q* are the frequencies of mutant and wild males, *P* and *Q* the frequencies of the females inseminated by them, the coefficients of mating success of the two kinds of males are $\frac{P}{p}$ and $\frac{Q}{q}$. the relative selection value K is P/p :Q/q. The variation of K as a function of the genotypes is given in fig.4 and 5. The disadvantage of *Bar* appears to be more important when its frequency in the population is above 50%. The results are more striking for white,which is at a disadvantage when its frequency lies between 40 and 80%, and at an advantage when its frequency falls below 40 %.

This advantage of the rare type was found in various species of Drosophila : EHRMAN demonstrated it between strains of different geographic origins, between lines selected for geotaxis and phototaxis, between lines reared at different ~~te~~ temperatures in *Drosophila pseudoobscura* (EHRMAN and al, I965; EHRMAN,I966; table 2). SPIESS demonstrated its existence in *Drosophila persimilis* (SPIESS, in EHRMAN,I965;SPIESS,I968;SPIESS and SPIESS,I969 b)(table3), EHRMAN and PETIT (I968) in the williistoni group (table 3), BORISOV in *Drosophila funebris* (I970).



Pair per chamber				Matings				Have mated				χ^2
No	A	B	Runs	A♀ × A♂	A♀ × B♂	B♀ × A♂	B♀ × B♂	A	B	A	B	
1	12 Cal.	12 Texas	7	29	21	26	28	50	54	55	49	[illegible]
2	20 Cal.	5 Texas	6	57	27	13	12	84	25	70	39	[illegible]
3	5 Cal.	20 Texas	7	13	17	26	48	30	74	39	68	19·91
4	23 Cal.	2 Texas	5	73	20	4	4	93	8	77	24	34·78
5	2 Cal.	23 Texas	10	4	8	26	62	12	88	30	70	65·76
6	10 Cal.	15 Texas	11	16	44	23	46	60	69	39	90	5·13
AR Mather, 16° *v.* 25°												
7	12–16°	12–25°	8	44	18	28	28	62	56	72	46	5·72
8	20–16°	5–25°	6	67	18	15	1	85	16	82	19	0·09
9	5–16°	20–25°	6	11	12	21	57	23	78	32	69	8·61
10	23–16°	2–25°	10	67	29	13	3	96	16	80	32	64·26
11	2–16°	23–25°	9	3	11	20	72	14	92	23	83	27·02

Table 2 - Numbers of mating recorded in observation chambers containing two kinds of D. pseudoobscura (from Ehrman,1966)



A	B	A × A	A × B	B × A	B × B	Z_i	Z_u	Z_r
Drosophila tropicalis, total number of matings observed = 3,200.								
5	20	60	119	92	126	747	2.77 ± 0.14	1.87 ± 0.12	1.36 ± 0.10
12	12	59	350	172	130	390	2.47 ± 0.11	0.82 ± 0.16	1.09 ± 0.07
20	5	64	743	104	114	113	2.66 ± 0.14	0.67 ± 0.07	0.61 ± 0.07
Drosophila willistoni, total number of matings observed = 1,986.								
5	20	29	48	92	140	360	1.16 ± 0.11	1.80 ± 0.14	1.18 ± 0.11
12	12	31	170	180	125	250	1.24 ± 0.09	0.76 ± 0.07	1.10 ± 0.08
20	5	31	381	146	96	43	1.08 ± 0.11	0.60 ± 0.08	0.92 ± 0.10
Drosophila equinoxialis, total number of matings observed = 1,892.								
5	20	43	67	98	114	351	1.45 ± 0.12	1.88 ± 0.13	1.62 ± 0.12
12	12	42	184	130	128	204	1.50 ± 0.10	0.94 ± 0.08	0.96 ± 0.08
20	5	54	308	149	91	68	1.24 ± 0.10	0.42 ± 0.06	0.68 ± 0.08

Table 3 - Summary of matings observed with different numbers of D. tropicalis, D. willistoni or D. equinoxialis (from Ehrman-Petit,1968).

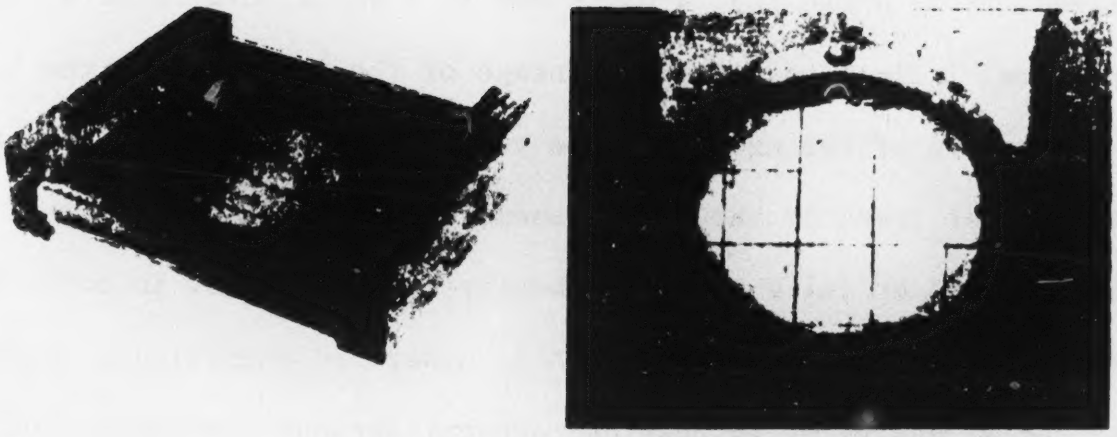


Fig. 5- Two views of the Elens Wattiaux chambers.

Unfortunately systematic investigations have been made in Drosophila only. Nevertheless, it is known that a black ewe in a white herd is mated first,a nd there are some indications of an advantage of the rare type in the human species. The charm of the exotic may be viewed as one of its manifestations... Following another trend of thought it seems difficult to believe that the oral tradition conveyed by fairy tales is absolutely gratuitous. In both, PERRAULT and GRIMM, the beloved hero or heroine is always an exceptional individual either in social status or in physical aspect. Serious anthropological studies should be undertaken on this subject.

It would be interresting to know the reasons for this curious phenomenon, but we only have a few indications. The problem involves the means by which females receive the information that allows them to choose one male instead of another. Actually this may be a wrong way of presenting the problem due to interaction between stimuli and response, the importance of the female level of receptivity, and possible competition between the courting males. Mating of females depends I) on male activity, the more active and efficient males being more successfull ,2) on female receptivity, that may, that may vary with the courtship that she"person~~n~~ally" receives, and on the general amount of stimuli emitted by the male population. Since the signals sent out by the males are essentially tactile, vibratory and olfactive, EHRMAN and PETIT tried to separate the different kinds of signals., by two different techniques.

ERHMAN studied Drosophila pseudoobscura using Elens-Wattiaux cages (I966) separated by different materials that allowed either odors or vibrations to pass trough. 25 pairs were placed in every cage and matings were observed directly and recorded. One of the cages contained 20 % of one of the genotypes, the other I00 %; a light current of air was channeled from the cage containing I00% to the cage with 20 %. When odors and vibrations were transmitted, the advantage of the rare type disappeared. This proves that the level of receptivity of the females was sufficiently lowered to prevent discrimining (EHRMAN,I966). The results of the experiments with either odors or vibrations were more

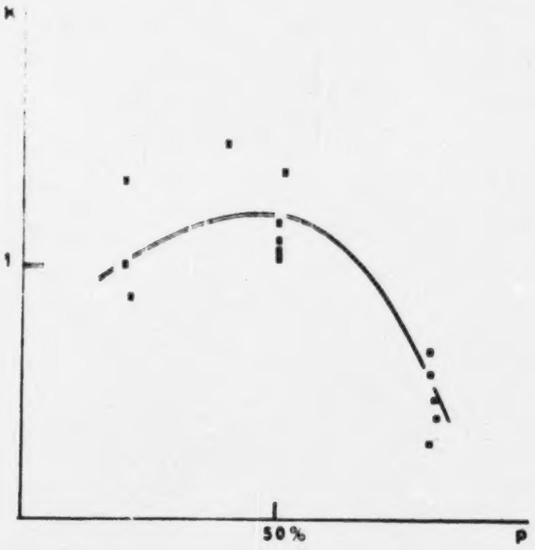


Fig. 6a

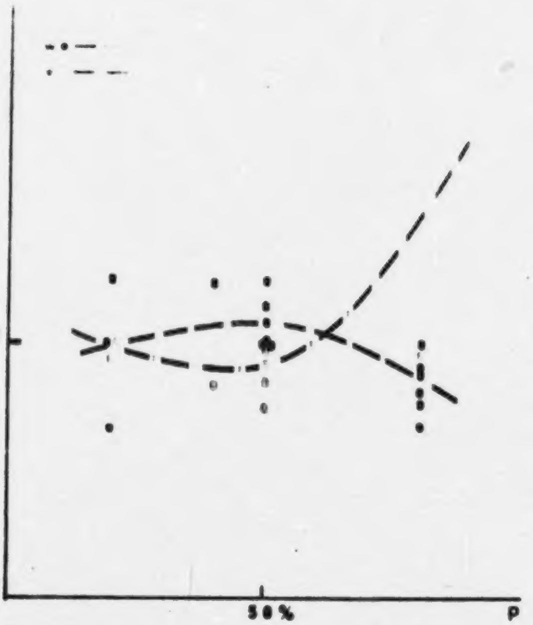


Fig. 6a'

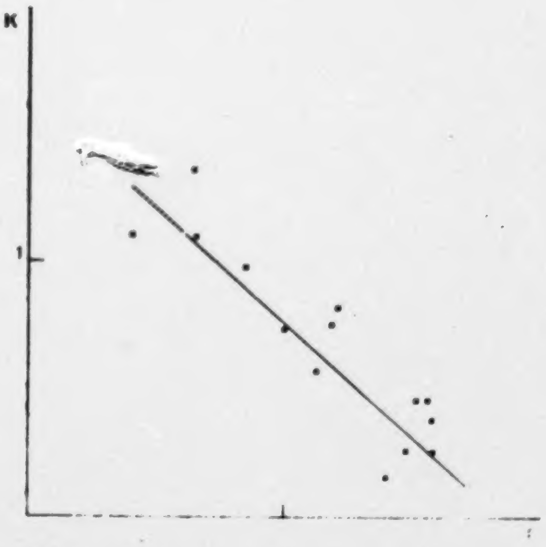


Fig. 6b

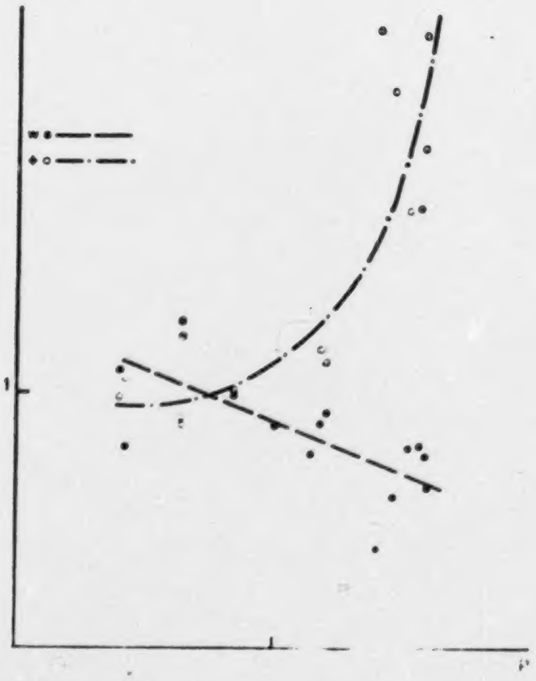


Fig. 6b'

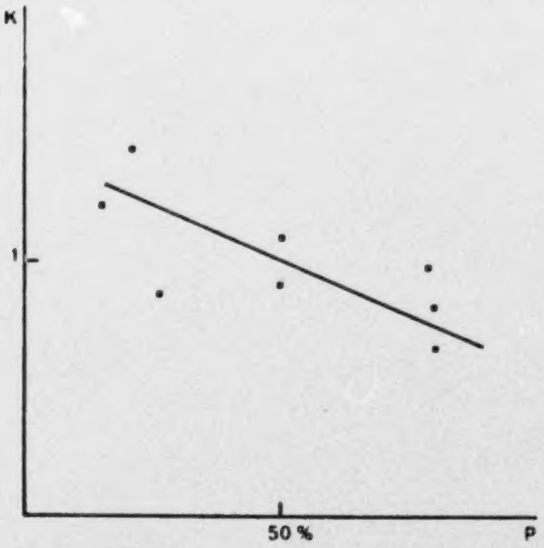


Fig. 6c

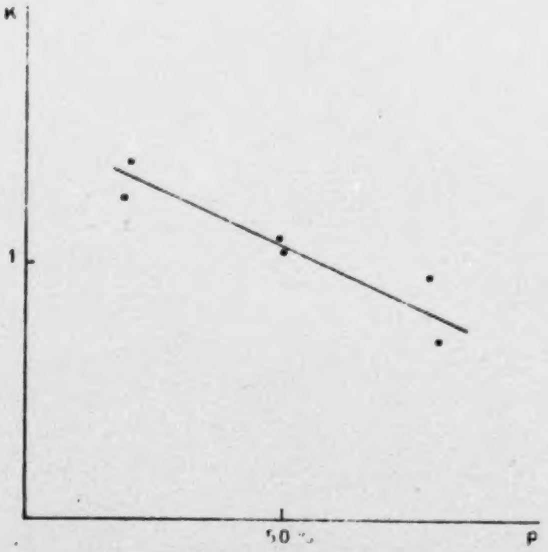


Fig. 6d

Fig.6- Frequency-dependent selection

6a :K
6a':P/p and Q/q } control experiments

6 b: K
6 b':P/p and Q/q } males without wings

6c :K males without wings, females without aristae
6d :K males without wings, females with neither aristae nor funiculi.

ambiguous (EHRMANI967,I968), as it is extremely difficult to transmit odors without vibrations.

PETIT (I968) taking into account the fact that in Drosophila melanogaster, the main receptors of females are on the antennae (cfp.6), destroyed the effectors of the males in the population, i.e. their wings, or the receptors of females which are composed of different antennary segments. The I00 pairs of flies in each experiments were operated upon during the narcosis necessary to separate the sexes on hatching. Two days later, they were integrated for 24 hours, without anesthesia. Females were then isolated in vials, and examination of their progeny, made it possible to determine the kind of male with which they mated. Coefficients of mating success and relative selective values were calculated. In view of the structure of the antenna (see fig.I), the ablation of the arista reduces the perception of vibrations, but leaves the perception of odors. Ablation of the funiculus suppresses the main olfactory receptors. If the part played by olfaction were important, the results of the two sets of experiments would be different. Fig.6c compared to the control (fig. 6a) shows that, without arista i.e. without vibration, the advantage of the rare type is not as important. Fig. 6d representing the experiments involving females without olfactive pits, is the same as the preceeding example. THerefore it may be concluded that olfaction has no influence at all.If vibration is essential, frequency-dependency would not exist with alarectomized males (fig.6b). Though very puzzling, this result may be partially explained as follows : I) the frequency of notum muscle vibration during flight is the same as the frequency recorded behind the fly (BENNETT-CLARKE and EWING,I968,NACHTIGALL,I966), so a vibratory stimulation may intervene with alarectomized males; 2) the direct observation of courtship (PETIT ,I958) proves that wild males circle around the female as they court them; so competition for space is strong, when white males remain practically motionless behind the females as they court them. Thus competition would essentially exist between males of the same genotype; it would be a kind of ecological competition. Such a conclusion, though logically satisfactory, must not be hastily accepted, as it has only been ascertained for one mutant and in one species.

Since the advantage of the rare type has been found, when there is no isolation, every time it has been looked for, this peculiar interaction of genotype with biological environment may well be a general phenomenon. In addition, this behavioral phenomenon may represent an important contribution to evolution by maintening polymorphism within populations.

CONCLUSION

All behaviour exhibits wide genetic variability, which is predictable when one considers the amount of polymorphism discovered during the last twenty years. All the consequences of the interaction between gene environment are to be added to this variability. For a genetici~~e~~st, they are considered to be one of the aspects of genetic homeostasis.

From an evolutionary point of view, the ability of a genotype to react to environment may be an advantage important enough to be selected during the course of evolution, so that the adaptative potentialities of behaviour improve and the influence of environment grows as the zoological group is more advanced.

When it comes to man, this ability may be attributed to a great polymorphism in the genetic basis of behaviour and intellectual abilities. The range of phenotypic polymorphism may be especially wide, as a result of the considerable level of evolution and lenght of development that has made the action of social and cultural factors even more important.

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FINAL DRAFT MINUS TWO (9/30/1971) -- NOT TO BE CITED

THE MEANING OF CRYPTOHOMUNCULUS*

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INTRODUCTION

In a very general sense, to many people, the cryptohomunculus is the destiny of each person--a destiny Grecian in its relentless, predetermined power to write the scenario of the individual's life. The earliest human thought, in all of the five cradles of civilization, featured the concept. Later, in the early days of science as it is thought of today, there were many proponents of the theory that the conceptus, or the foetus, was a miniature adult whose every characteristic was set, either by virtue of the blood of its ancestors, or some mystical force. Some, like Hildegard, the German clergywoman, thought that the particular essence of the father and the particular essence of the mother had been chosen for union in heaven and these were then implanted in the mother's womb thus continuing parental characteristics in the offspring (Sarton,).

There are many today who have modern formulations for the same type of performationist schemes. These schemes vary in many ways but they are similar in their insistence on the controlling, limiting, determining role of an "essence" that is in the zygote. The discussion of these formulations in the various scientific institutions of our nation and in the public forums available to scientists has engendered much concern about the social and ethical implications of this seemingly "purely scientific" concept. I think that at least three "meanings" of the cryptohomunculus cannot be ignored, i.e., its social meaning, its scientific meaning and its meaning for the strategies and tactics of research.

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* T. C. Schneirla and I were to have written a paper with this title for a conference on the Biopsychology of Development (Tobach, et al.). The plan was never carried out because of his untimely death on August 20, 1968. Many of the ideas expressed herein stem directly from his protean theories, and my debt to him will be evident. My use of the title is meant as a tribute to him and I hope that the deficiencies in the paper will not detract significantly from that expression of honor and gratitude.

I. Assumptions underlying the organization and content of this paper

The group meeting in conference here is well acquainted with the experimental literature dealing with the genetic and environmental factors relevant to behavior in human and infrahuman animals; they are familiar with significant review articles, books and symposia. They are also aware of the extensive discussions and controversies engendered by these writings.

Although there is no programmatic statement from any group of writers which may be said to represent a consensus, a discussion of the most controversial issues raised may be helped by a listing of some of the representative and some of the conflict-producing tenets expressed. In doing so, there is no intention to overlook the differences that exist among all those who have written on the topic of the conference.

1. All disavow any desire to harm any ethnic group, genetic population, or "race." The issue of genetic endowment is raised out of a genuine desire to put the findings of science in the service of improving life for all segments of the population. The findings of science may be contrary to the popular thinking of some segments of the society, but by facing the reality, priorities of time and other resources may be ordered in the most efficient way.
2. Although human learning ability, intelligence or other cognitive forms of function are affected by environmental factors, the genetic basis of these behavior patterns limits the extent to which training can alter performance in these areas.
3. Data from behavioral research with infrahuman animals, biomedical research with human beings and evolutionary theory support the thesis that various human genetic populations are at different levels of evolution, because particular genetic populations show differences in patterns of motor and sensorimotor development. These interpretations are considered further evidence of genetic limitations that cannot be overcome by environmental treatment.
4. By democratic means, society can be brought to understand and accept this interpretation of the data and voluntarily organize societal programs to improve the genetic characteristics of society. As far I have been able to determine, "society" is restricted to mainland United States.

Some of those involved in the discussion categorize various parameters relevant to behavior as belonging to either the genetic or environmental class of factors. The reaction to this dichotomization is extremely varied. This may be the critical issue requiring theoretical resolution.

Some are primarily concerned with determining the relative valence of one or the other class of factors in the genesis of a particular behavior pattern or a particular structure. Some formulate the relationship between the two as an interaction, requiring that either be held constant so that the other may be varied to elucidate the effects of the one on the other. Some state that genetic considerations may be dismissed once they are undestoood. Others see the concepts of environment and heredity as abstractions of a developmental process in which genetics and environmental factors are all part of the to experience of the organism.

Much material relating to the arguments about methods and operations of the research leading to the issues under discussion has already been published. These are operational problems that can be resolved by other experimental and mathematical operations.

Some findings will probably not be disputed here. There are individual differences in human structure, physiology and behavior; there re group differences among humans in structure, physiology and behavior; there are genetic populations describable in terms of particular genes and their frequency in any human group; there is a greater or lesser gene flow between human populations; genetic processes are fundamental to all aspects of living organisms, including their behavior. There will probably be the most disagreement about the role of these genetic processes in the highest level of behaviora integration known to us at present: the behavior of human beings in a technologically complex society. Except for comparison, other types of society have not been discussed.

II. Personal biases and operational guidelines

It is important that scientists be aware of the setting in which they work and publish, as well as of the theoretical and other biases affecting their work.

This does not prevent one from being biased without awareness. When the interpretations, conclusions and interferences about a scientist's concept of reality are tested and found wanting, the original work must be discarded and new work done to generate new hypotheses. This is most feasible in the physical sciences whose findings are most frequently tested via the technology developed as a result of such research. This is most difficult in those sciences where people and their behavior are concerned.

Scientists are human beings, a species that has developed various cultural systems about the propriety and desirability of certain patterns of behavior. These systems are continuously changing. Discussions about which of the current value systems are the best are always functions of the individuals engaging in those discussions. It seems desirable for scientists in the United States in this year, in the world as it is today, to be conscious of their thinking in this regard and to make some effort to state their understanding of the particular value systems they abide by. This is not a new procedure in the area of society-scientist relationships, as the earliest recorded history testifies (Sarton, ; Needham,).

I do not foresee that I will be able to present some novel, creative analysis of the existing experimental and theoretical literature that will resolve the issues before us. My own level of competence is such that I prefer to attempt to deal with what I consider the basic, underlying assumptions of the controversy in general, whether they are explicit or implicit, and to delimit my area of discussion thus because of my own shortcomings.

It is not possible to talk or write about the assigned topic without making appropriate statements about the biases with which I start out. I do not consider this an "unfortunate imposition" or "dictated" by the nature of contemporary societal pressures. I am not crying "*mea culpa*" in order to absolve any errors in judgement or fact that I may have made or may make. I am trying to do as I would have others do, so that we might arrive at some agreement about how to formulate the question under discussion so that our consequent activity both in the scientific and larger societal community may be constructive in order to achieve the goal to which we all strive: accurate knowledge about reality, shared with all of society so that it can define problems accurately and make appropriate decisions to solve those problems, in such a way that the best interests of most people can be served, after the people involved have been convinced that the formulation of the problem is correct and its solution is desirable. It is important that such discussions by individuals and groups take place as openly and as vigorously as possible. I welcome this opportunity to participate in this particular discussion, and am flattered and honored by the invitation.

The following points may be or may become tangential issues in the discussion. I wish to make some statements about them in an attempt to prevent this.

1. Although I am critical of some formulations of the role of genetic processes and environmental factors, I recognize the necessity and desirability of investigations of the genetic processes and their relationships with all other aspects of biological function in all species.
2. Although I reject the formulation that one group of people is inferior or superior in regard to any other group of people, I recognize differences among and between groups, or among and between individuals, that may be related to differences in those biochemical systems we call "genes."
3. Although my social value system does not condone some of the formulations described above, I am not desirous of legislating the type of research done on that basis. Society must find its own ways for determining what research should be supported by it. It cannot and should not prevent private individuals from doing research that society does not wish to support. However, in both instances the processes by which both occur--

that is, the decision to support research or not to support research, or to prevent individuals from doing such research, should be open to free and public discussion so that the decision-making process is not used against the common welfare or to persecute an individual outside of legal constraints.

This last aim for the logistics of research may be desirable, but it is not always achievable. It is the human condition to be constantly engaged in attempting to achieve this goal and to be variably successful in achieving it. However, the basic premises and assumptions underlying the research and the applications of the research findings need to be continually evaluated and challenged. This is one of the most important processes in science, and the desirability of engaging in and encouraging this practice and training new scientists in the methods of doing this cannot be overemphasized.

I see at least three main questions before the conference. While they are isolable for purposes of discussion, they are interrelated, and the interrelationship needs to be explored as well.

1. The formulation of the scientific problem. The conference organizers have proposed that it is "Genetic Endowment and Environment in the Determination of Behavior." I would like to propose that this formulation needs to be re-examined.
2. The logistics of research in the problem area. How shall the priorities be determined in an era of economic restriction and societal conflict? I would like to propose that a proper discussion of this aspect of the conference would involve other experts in addition to biologists and the particular behavioral scientists here now, such as philosophers, historians, sociologists,

economists, social psychologists, and anthropologists. Or, is scientific strategy independent of such considerations?

3. The relationship of the scientific problem to society.

It might also be helpful to state some concepts that I consider fundamental to the material presented here.

1. Science deals with causal processes in order to reflect reality efficiently. Explanation is defined in terms of process, i.e., what is acting or working in what way, on the basis of past events; leading to what future events, that are related to what currently acting processes, and having been related to what other processes in the past; and that may relate to other processes in the future. How are all of these acting to bring about change? Other types of explanation, e.g., operational, correlational, sequential are temporarily useful but not sufficient.
2. The concept of levels of organization and integration is a useful tool for the formulation of testable hypotheses about phenomena and the integration of data gathered through such investigations to permit better understanding of the causal processes responsible for those phenomena.
3. Schneirla's concept of behavioral development as a function of phylogenetic and ontogenetic processes is a helpful application of the concept of levels of organization and integration to the study of behavior.

SOME QUESTIONS FOR DISCUSSION AT THE CONFERENCE

I. The formulation of the scientific problem

Certain statements seem to be fundamental in their need for consensus.

Genes do not function in vacuo; the evolution of the first biochemical molecule was inextricably involved with the milieu in which it achieved an entity of its own different from any other entity in the surround. One cannot discuss genes without stating the context or milieu in which their function is expressed. Genes function on a biochemical level, expressing that function in biochemical systems, such as various proteins, enzymes, etc.

All configurations of living matter have some developmental relationship to genes. All configurations of living matter cannot function in vacuo but are in constant energy-transformations with the surround which becomes internal; during these energy-transformations, the surround is also changed as a function of internal organismic changes.

Behavior is an ordered set of phenomena derived, based on, or in some way relatable to physiological function and to the structural characteristics of the organism involved.

Behavioral patterns may be analyzed in terms of component bits or subpatterns.

Species and individuals show similarities and differences in total behavior patterns, as well as in the component bits.

Behavior, like all other biological phenomena, is a function of genetic processes.

Behavior, like all other biological processes, is a function of the constant energy-transformations with the surround.

The genome is not a homunculus that grows to adulthood. The "Behavior" is not in the genome. Between the biochemical expression of gene function and a behavioral pattern, there are many intermediate steps and functions on different levels of organization. Mendelian methods and biochemical methods involving the isolation of particular gene functions that may have some direct or indirect relationship to a behavioral pattern or item are two valid approaches to understanding the relationship between gene function and behavior. The situation, circumstance or environment in which genes are expressed or in which behavior is studied is an essential factor in understanding the relationship between gene function and behavior.

Genetic processes as we know them can best be described functionally as the expression of a particular biochemical process derived from a particular nucleotide configuration in a particular setting. This biochemical process may be expressed as enzymes, structural proteins, ribosomal or transfer ribonucleic acid and as regulatory substances. A very specific biochemical action or a structure can be traced to a specific gene or group of genes.

Behavior itself may be ordered in terms of complexity, number or component structural and functional elements, patterning, temporal factors, situational factors (e.g., individual interaction with physical aspects of environment or individual interaction with other organisms in relation to physical aspects of the environment). To subsume all these variations, behavior may be described as the action of the individual organism as an integrated totality in relation to the environment in which it is located and in relation to the internal state of the organism. This action may involve movements of the entire organism as a whole or a part of the organism. The partial action is always a function of the total organism in its environs.

In discussing the relationship between genetic processes and behavior, it seems desirable to analyze the behavioral pattern or item in regard to its relevant anatomic and physiological substrate. The analysis would require suitable investigation of the pattern under all relevant conditions of the organism, and all the situations in which the patterns can be observed, as well as the development of the pattern during the life history of the organism. Comparison of species, strains and other subgroups would also be useful in fully defining the pattern being analyzed and in relating to the anatomical and physiological processes which are more or less implicated in the behavior pattern.

A complete analysis of the behavior pattern and its lower level substrates would proceed to each preceeding level, including that of the specific gene action. Because gene action is most fruitfully studied developmentally, the synthesis of the processes uncovered by the analysis outlined above could now take place by integrating each level of organization in the succeeding levels, during development of the organism. As in the case of the behavioral analysis outlined above the techniques and principles employed in each level would be particular to that level.

This plan of action has already been carried out for some behavior patterns for some species to some extent (Ewing; Rodgers; Schlesinger and Griek; Hirsch; Ehrman;). The plan is derived from the concepts generated by the work and writings of the classical geneticists, students of behavioral-genetic analysis, developmental geneticists, and the concept of behavioral development.

In most of the formulations about the roles of heredity or genetic endowment, and environment, the term "interaction" is used. Depending on the level of organization in focus, "heredity" and "environment" need to be redefined, and it is always possible to separate abstractly the two classes of phenomena. At every level, the "interaction" is changing and fusing into a "new" genetic-functional substrate (e.g., from nucleotide arrangement, to enzyme, to cell producing a particicular secretion) which is in a new relationship to a new "environment." The events at one level of organization at one point in time is the substrate from which the next developmental sequence is generated. As the changes between levels become incorporated, the original configuration changes its relationship to the level under focus. The change is not additive--it is a change in quality as well as in quantitative aspects.

Another characteristic common to many discussions about "heredity" and "environment" is "typological thinking." (Dobzhansky; Mayr; Hirsch) This has been excellently discussed elsewhere and needs no repetition here. It seems to me that "typological" thinking is characteristic of some discussions about evolutionary processes as well.

The relationship between ontogeny and phylogeny has been widely discussed particularly as a possible clue to understanding evolutionary processes. Several writers have commented on the hierarchical arrangement of phyla or species in a scale of increasing complexity apparently correlative with evolutionary age. Some have gone further (e.g., Noble) and attempted to make the same type of correlation within species, particularly human beings.

It is possible to order phyla, or species, in terms of particular aspects of function, such as behavioral plasticity of the nervous system. Within any particular phylum, or subphylum or class, it may be possible through behavioral studies to hypothesize how these species may have been related in evolutionary history to some common ancestor. However, no contemporaneous species may be termed generally "superior" to another, insofar as species have survived through various evolutionary processes to occupy ecological habitats in which the species is supported.

Great variation in developmental patterns is also found not only when phyla are compared, but even when suborders are compared. As Nice has illustrated in the analysis of developmental patterns in birds, precociality or altriciality, as a stage of maturation at hatching needs to be specified in regard to physiological or anatomical systems. Altriciality or precociality is not absolute, as different systems mature at different rates. This is also true in mammals, as for example, in the order rodentia. In this group of animals, there are many types of developmental patterns, as regards stage of development of sensory or motor function at birth. The guinea pig, an outstanding example of precociality in this order is born with eyes and ears functional at approximately the adult level in most practical regards, and fully able to locomote. The laboratory rat is primarily altricial in regard to motor, visual and auditory systems, but apparently "precocial" in regard to olfaction and tangoception. Among all the species in the order of rodentia, it is not possible to arrange rigidly the species in regard to behavioral plasticity and developmental pattern. In addition to the definition of situations which may be considered comparable in order to define a behavioral continuum (Hirsch), the need to determine which systems shall be used as the basis for comparing development pattern and rate has not been resolved (Tobach, et al).

As Gottlieb has pointed out, a comparison of the patterns of sensory development can point to possible relationships among various classes ( ). But it has not been demonstrated that the relationship between rate of development of motor or sensori-motor systems is significantly correlated with behavioral plasticity within a species. In the order of primates, such a general hierarchical statement can be made comparing prosimians and anthropoids, but it is difficult to do so within the anthropoids. Certainly, it is not possible to do so in a correlational respect between motor development and general behavioral plasticity. A comparison between people and subhuman primates would seen to support the correlation between motor development and behavioral plasticity, but it is clear again that the phyletic classifications are between suborders, not within species. One might attempt to correlate behavioral difference and evolutionary age, as in the case of aplacental mammals (metatheria) and placental mammals (eutheria), which present very different developmental patterns, and possibly different levels of behavioral plasticity (such differences have not yet been determined fully) and arose in different eras (cretaceous and eocene respectively). To generalize from this about equivalent relationships between other suborders of mammals, or genera is possibly an example of a kind of "typological" thinking. The attempt to make such generalizations about the evolutionary relationship of different human populations in terms of motor development and "intellectual" development is another example of this kind of thinking.

The experimental concepts used in developmental genetics also seem applicable to the understanding of the relationship between gene function and behavior. The study of behavioral development has proceeded for the most part on the molar level, that is, changes in behavior with growth and maturation of the entire organism. When development is viewed as a process in which the total experience of the animal during its entire life history is the agent for change as seen in growth and maturation, there can no longer be an artificial separation between the biochemical functions attributed to the genome and other types of experience. In Schneirla's conceptualization, experience includes all levels of organization and integration, with no exception. The statement is only the beginning, however. The meaning of the statement is seen in the plan for analysis and synthesis of fundamental processes in behavior suggested above.

In the case of the most complex type of behavior evidenced by the most complex organism known today, that is, cognitive function (including creativity) in human beings, the problem of analysis of the behavior into its component parts which might be traceable to specific gene action is still before us. In the case of performance on a particular test, such as the Wechsler-Bellevue Intelligence Test, the analysis of the behavioral patterns involved in that performance has not bean carried out.

It may be argued that there are two valid methods for attacking the problem of the development of behavior by the study of genetic processes: the classical Mendelian analysis as well as the molecular analysis of gene mechanism. It is not quite clear how any of the studies done to date present us with information about the identifiable behavioral bits going into the pattern which might be called "I.Q. test performance" or "cognitive function." There have been a number of excellent papers (   ) questioning the validity of considering test performance as a heritable trait (i.e., genetic trait or character). Indeed, those who are concerned with the relationship between "environment" and "heredity" in test performance are correctly cautious in indicating that it is not known what is being inherited.

It would appear that such an analysis would be primary to understanding gene mechanisms in this behavioral pattern. Assuming that such an analysis under the appropriately varied conditions, at an adequate number of developmental stages, in an experimental design permitting some basis for generalization about a particular population has been carried out (Hirsch), the task of analyzing the physiological and anatomical substrate, through further basic levels of organization and integration needs then to be undertaken. Assuming then the isolation of appropriate gene mechanisms, the process of synthesis during the development of individuals in the population is necessary.

The problem of synthesis becomes most difficult when dealing with the human species. One of the remarkable events in the evolution of animal species is the increasing independence of the species from the environment, as increasing neural plasticity evolves (Dobzhansky). The contemporaneous end-point in this hierarchy is the human being who alone among all species can most creatively control its own environment. Thus, the possibilities of different environments in which the synthesis of the development of individuals can take place is immeasurably increased; we cannot predict the future environments in which people might live. This experimental difficulty has a positive aspect: in view of the fact that we have this ability, we can presumably make use of existing knowledge to create an optimal environment to achieve goals we set for ourselves. Our problems are not thereby reduced, but their nature is significantly changed in regard to the problems before this conference.

Depending on the behavioral item under analysis, the levels of organization beyond the molar, individual organismic level vary significantly in relation to the species (the phyletic history of the organism). In the instance of the human being, the behavioral pattern "test performance" is a social behavior pattern, as is all human behavior. It is necessary now, on the level of human social behavior, to deal with the phenomena peculiar to that level, namely, societal, cultural phenomena. The behavior of the individual cannot appear *in* vacuo.

How might the concept of levels be seen in the behavior of an individual human being in regard to complex, cognitive function during an I.Q. test? If the brain of a human being is deprived of oxygen, the physiological basis for congitive function becomes a primary factor in determining the quality of cognitive function in an immediate, contemporaneous fashion. Regardless of the past experience of the individual, the cognitive function of that individual is extremely low. Cognition itself is a process which may be organized by increasingly complex orders of behavior. As one progresses through successive orders of cognitive function the quality of other factors, as well as their quantitative nature, become more relevant. Thus, the ability to derive a statement in calculus is a function not only of the physiological experiential history of the individual but the social experiential history of the individual. How much and what kind of mathematical training did the person receive? Cognitive function, like all function of the individual organism is always a derivative of all levels of function, physiological, behavioral and social.

It should be pointed out that the concept of levels of organization and integration in itself sets no restriction as to the level that is validly studied. Any one level may be extremely fruitful as the focus for the analysis of behavior. Thus, it is as useful to study the performance of an individual on the molar behavioral level, in regard to the processes involved in cognitive function, as it is to analyze structural and physiological substrates, or social factors in cognitive function. The need to involve other levels of organization stems from the kinds of questions asked; if causal processes are sought, or if gene mechanisms are being investigated, the levels become varied.

Perhaps the problem is what are the appropriate levels for dealing with the relationship between physiological (or biochemical) psycho-societal phenomena on the human level? In this discussion, the psychological and psycho-societal levels are separated out for discussion and analysis. In reality they are fused in any particular behavioral, physiological or anatomical phenomenon under discussion. In talking about the human level, we are also considering the human level as one phyletic level, which shares much in common with other phyletic levels. At the same time, human beings present a new level in behavioral integration by virtue of particular species characteristics, such as language, history, and culture.

On the human level, physiology and psycho-societal phenomena stand in a hierarchical relationship to each other. While physiological function is the sine qua non for all other functions (a sick human being cannot function in the same way as a well human being), human behavior is psycho-societal. In addition, as with any behavior, one needs to consider that at early stages of development the physiological processes of growth and maturation, derived from the fusion of experience at all levels of individual function, may play relatively more important roles than the psycho-societal, which may operate indirectly. Protein deficiency in a parturient woman, or protein deficiency during the early development of the parturient woman, may result in relatively permanent impairment of neural function in any children born by that woman. It is obvious, however, that the protein deficiency itself might be a psycho-societal factor as well as some enzymatic deficiency in the woman, as a result of a genetic expression during her own growth and development. In the context of the levels concept the medical treatment of the protein deficiency carried out on the physiological level is within the psychosocietal context.

The consideration of individual differences is extremely important. The problem for the conference seems to be: how do those differences come about? How are we to approach the problem of analysis of behavior, with its underpinnings of physiological and other basic phenomena, as well as societal processes? The behavioral scientist needs to identify the problem and formulate questions about the problem which are answerable by experimental investigation. It is extremely necessary, however, for the behavioral scientists to recognize the boundaries between levels. Some phenomena needs to be analyzed in the context of societal processes with the appropriate societal techniques, principles, theories and procedures. Others on the individual level need to be studied by means of biochemistry and other tools of the physiological armamentarium.

In light of the extreme complexity of the problem as formulated above, and the complexity of the research plan proposed, the question of logistics becomes paramount. Indeed, a frequently heard comment about Schneirla's theories is "But it's so all-encompassing that no one person could do it." I think that is true; but there are possible ways of dealing with that aspect of the logistical difficulties involved. The logistical question that I think needs consideration here is quite different.

II. The logistics of research in the problem area

An important issue that some may think has obtruded itself is the feasibility of doing research in this area because of the intense societal concern with the implications of the research. I would like to pose some questions for discussion in this regard.

Is an individual's scientific strategy independent of the societal milieu? Are scientists free to pursue "truth" wherever it will lead them? Does the scientific "ambience" affect the course of an individual's research? Do considerations of economic restriction and societal conflict play a role in an individual's strategy of scientific research? Are scientists the ultimate decision-makers in research strategies?

I would like to suggest that the problem might be formulated as follows:

People should be free to question all and any preconceived or established ideas. This is true in the societal sphere as well as in the scientific sphere. For example, it is the right of non-scientists to question what scientists believe and to question the priorities that scientists set up for themselves. Who shall say how the national budget should be assigned in regard to research or services?

Scientists also have the right to answer freely and without restraint any questions they may have. But scientists, just like the society in which they are part, should operate within an ethics system that governs all people, regardless of their type of work. When we say that the society has a right to question the status quo and even change it (see the Declaration of Independence) we expect them to do so without endangering the lives of the people, without circumscribing individual freedom and without the dehumanization of people. Scientists similarly are constrained. The research done with captive populations by the Nazis, or by certain unscrupulous scientists in our prisons today, or on our "mental retardate" wards is similarly to be criticized as in the way we would criticize people who wish to change society without regard to an acceptable ethic. The ethics of behavioral and medical research is quite another aspect to this second level of research and again it is questionable that biologists only should be involved in that decision. What is the most important contribution that scientists can make? One criterion that is generally acceptable is that the knowledge must be testable and in consonance with reality.

How shall the scientists and non-scientists relate to each other in regard to the questions and formulations raised above? Can the levels concept be helpful here? When the scientist's work becomes part of human culture as ideas, inferences, theories, and basis for societal action, the scientist is but one participant in the societal process of decision-making.

It seems desirable to start from the premise that all people have the right to be told all that the scientist knows in order for society to define its priorities in line with its value systems. It is equally necessary for the scientific community to inform all people about what it is not sure of, what it has doubts about and of the controversies and disagreements that scientists have among themselves. The scientist may be as wrong in doing scientific work as any non-scientist may be in doing some other kinds of work. At least, one important factor that operates in both cases (scientific and non-scientific work) is the directness of the negative feed-back. If Boyle's law is incorrect, one cannot devise an effective machine based on that principle. The scientist in that instance is immediately required to re-investigate the basic premise, i.e., Boyle's law. Similarly, if the non-scientist operates on a principle that defies or negates reality, at the same point a change in the basic assumptions underlying the behavior involved has to be reexamined. In all these instances the efficiency and accuracy with which these operations are carried out are a function of the many factors which are involved in behavior in general, either on a personal level or on a societal level. Profound mistakes in the judgement may be made, and the processes by which these mistakes are made and avoided are complex and worthy of much discussion. The scientist at this st of human history has as little basis for understanding those processes as has any other member of the human population.

III. The relationship of the scientific problem to society.

If the conference considers this question meaningful and worthy of discussion. It would seem that it is necessary to have a clear understnading of the relationships among the pursuit of scientifically valid research, the interpretation of the facts gathered in that way and the use of the facts on the interpretation of the facts. A case in point is the argument posed by one scientist who attempted to integrate the "scientific facts" with a social value system that appears to be contradictory to the "scientific facts" (Herrnstein). As an exercise in understanding the point I have presented, I would like to pose the following question:

How does one resolve the dilemma posed by the following;

a. If the environment is made equally affluent for all, it will give heredity more valence in leading to a class society based on inherited ability. Each person will not have a equal chance to succeed because of genetic endowment differences.

b. If environment is not improved in an eqalitarian manner, each person will not have an equal chance to succeed because of differences in genetic endowment, and because of possible biases in the environment.

Before attempting a resolution of the dilemma, it may be helpful to outline some concepts that may be generally acceptable.

There are rules arrived at by consensus in the scientific community about the gathering of scientifically valid data.

There are mechanisms available for discussion and the possibility of arriving at agreed upon interpretations with the understanding that those agreed-upon interpretations are always open to challenge and further modification or refutation.

The use of the results is a function of societal processes in which the scientist may or may not play a role.

Some of the problems that arise despite these guidelines may be described as follows:

Rules of scientific validity and reliability have been violated or not followed adequately.

Challenging interpretations that are widely accepted is not always possible because challenges require experimental support, thus involving societal aspects of scientific investigations (research funding, facilities, etc.)

Involvement in societal processes by scientists is not universally acceptable.

It appears to me that the use of facts gathered in research is a critical question before us. If scientists do not involve themselves in those societal processes which directly affect their activities they have few options open to them. It would appear to be imperative that scientists participate in all aspects of society in order to bring about an effective and desirable relationship between their work and the use to which it is put by society.

The scientific community has another problem before it, it seems to me. Those scientists who conclude that it is critical that gene mechanisms be understood, so that genetic processes can be dismissed when the behavioral patterns of populations are being considered, need to clarify how they reached such different conclusions from those scientists who also state that it is critical that genetics be understood so that steps may be taken to affect the genetic pool of certain populations.

This latter group proposes to do so by eliminating certain genes from the population pool by encouraging non-breeding, as by bonuses for sterilization (Shockley). Another proposal is not as clearly stated, but it may be inferred (Herrnstein) as follows. Genetic differences create classes. Those with the "genes for being unemployed," or in another sense, with "genes that permit retraining and thus survival in an increasingly complex technologic society" are continually pushed down in societal rank, and thus eventually are eliminated from the genetic pool of the total population.

This last proposal suggests that various tests be used to make a "more humane and tolerant grasp of human differences...possible...(because) the biological stratification of society would surely go on..." (editorial rearrangement, ET) This recommendation is based on a view that societies will always be based on competition among people. The nature of the competition is not characterized, i.e., whether it is one which is a fair-play, good-of-the-group competition, or whether it is a competitiveness that is negative and destructive towards others. The only clue in the proposal is the statement that "Human society has yet to find a working alternative to the carrot and the stick." (p. 64) It appears to me that it would be difficult to envisage a society, given a competitive value system based on the "carrot and the stick," in which equal opportunities would be created for obtaining training. Within some level of "humane-ness and tolerance," certain individuals from any stratum in society would be given the training required for them to succeed in a technological society. These people would then be able to contribute their genes to the pool of the population for further improvement of the gene pool.

Certain questions are raised by this proposal.

Who will define the humane-ness and tolerance with which the tests will be administered and interpreted in order to gauge human potential and performance?

It may be inferred from the author's statement that this is for society to determine. However, if human society will always be based on competitive motivation, how will this be eliminated from the decision-making process? Presumably, those with the "intelligent genes" from the lower classes who wanted a say in the decision-making process would rebel and thus participate in deciding the administration. The concept of class mobility is supported, as is the desirability of the removal of such social and legal impediments to innate human differences as "race, religion, nationality, title, inherited wealth." The impediment of sex is not included in the list.

Should some humane and tolerant means other than testing be used to guarantee that biological determination of success would take place?

What would be done with the "precipitated-out-of-the-mass-of-humanity-low-capacity (intellectual and otherwise)-residue that may be unable to master the common occupations...?" (modified by E.T.)

If biological stratification has been a feature of all past societies, is a feature of all present societies, and will be a feature in all future societies, what is the purpose of the humane,tolerant grasp of human differences that would be brought about by testing? What is the hope that would be fulfilled?

FINAL STATEMENT

What is the meaning of the cryptohomunculus? The prefix "crypt" could refer to what is hidden in the little person; to the fact that the person is hidden in something; or that the person needs to be decoded in order to be understood. What is hidden in the cryptohomunculus? No one would deny the existence and the necessity of the material transmitted from progenitor to the progeny; that is, that without the material being transmitted, there is no progeny. But, that is probably not the hidden aspect of the miniature human being, the mystery. That is the sine qua non of all matter, animate and inanimate. Every phenomenon has a history.

The little person is hidden in the organism, at every stage of development. In the case of sexual vertebrate reproduction it is in the sperm and in the egg. Neither of them are organized structurally or functionally to look or act like the zygote. The embryo, the foetus, the neonate, the juvenile, the adult, never look or act exactly like the individual will look and act at a later point in time. The rate of change will vary; the number of factors becoming dissimilar will vary; the number remaining relatively stable will vary; but at no time is the individual the same as it was a moment ago.

But, one might say, there are some elements which stay the same from the stage of sperm and egg, and are always identifiable as the same both in structure and function. These are genes which either endlessly replicate themselves in cells that are continually dying and becoming reborn or genes which do not replicate themselves but remain structurally stable and continue to function as de novo.

These stable systems are considered by some to be the hidden destiny of each organism.

However, at the present state of our knowledge, unless certain characteristics of the milieu in which these units function are altered, eventually those "stable" units will lose their identity.

Hidden in the little person is the future of the little person. This meaning of the cryptohomunculus is the critical one: to understand the organism,--its structure and behavior,--it is necessary to unravel its history, to determine how the various levels of organization were differently integrated in time to bring about what was observable at any point in time. The "little person" is the last stage before the next; it has within it the possibility of going on to the next stage. The "inside" and the "outside" necessary to bring it to the next stage is what has to be "cryptoanalyzed." The message is clear. The solution is difficult.

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THE FUTURE OF HUMAN BEHAVIOR GENETICS

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THE FUTURE OF HUMAN BEHAVIOR GENETICS

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As a critic of Science Fiction has said: it is difficult to prophesize intelligently, especially about the future. In trying to guess what the future of behavior genetics is going to be, it is well to keep in mind that those who are in a position to influence the course of events make the most successful prophets. Some knowledge of the history of science also helps. Unpredictable serendipity has led to major breakthroughs in research but the ability to exploit such events required considerable knowledge of the existing science.

In this overview a distinction will be made of what should happen, in terms of research that is "central" to behavior genetics and what is actually likely to happen. We will also consider more "peripheral" or "auxilliary" research that is needed if behavior genetics is to advance. In all of this the approach will be a rather pragmatic one, which resembles much of modern psychology in its emphasis on techniques and empirical facts. Near the end a more theoretical problem will be posed. Finally, in an appendix, a test battery for use in cooperative studies will be suggested.

Let us first look at research that is somewhat less likely to happen but which should be encouraged:

The multiplicative value of multivariate analyses has been advocated by me before (Vandenberg,1968), but has only been applied with twin data. It should next be applied to parent-offspring data and genetic abnormalities.

In some studies of rare genetic diseases it has become a fairly common practice to combine data on patients seen in a number of locations or even for investigators to adopt a common set of diagnostic procedures in order to obtain a sufficient number of probands for a meaningful analysis. Behavior geneticists will also have to find a way of doing more cooperative research: either a number of them will have to do cooperative studies or they will have to find ways of reporting on a small number of cases in sufficient detail to permit future integration of a number of such reports.

A good example of what can be accomplished in this way is the summary by Moor (1967) of the effects-on the global IQ-of various types of sex aneuploidies from which I have constructed the graph shown in Figure 1.

If the individual investigators from which these cases were collected had used a common battery of short tests of different abilities and had also obtained data on the performance of parents and sibs on these measures, an even more informative analysis could have been made.

In a recent paper, Berman, J.L. & Robin Ford, (1970) performed a study in which they predicted by a multiple regression equation the intelligence of childr affected with PKU from IQ measures of parents and sibs. Then they related the difference between the predicted and observed IQ to blood phenylalanine levels. In children with truly elevated levels there was a larger drop from the expected I

Practical application of Ray Cattell's ingenious MAVA method (1953,1960, se also Loehlin, 1965) which calls for information about unrelated children raised in the same home, twins reared apart and other unusual situations, or the more conventional method of family studies involving more than two generations of interrelated nuclear families will also require such cooperation. Still other examples are furnished by studies of the rarer types of aneuploidies such as XYY or XXY.

We need more studies of adopted children and those in more detail than the one of Skodak and Skeels (1949), further analyzed by Honzik (1957). While social agencies may be resistant to a single investigator mounting a frontal attack, perhaps a more personalized search for single cases by a number of individual behavior geneticists will encounter less organized resistance. Similarly we need studies of children born to parents who were married more than once. Again, an accumulation of cases by a number of separate investigators may be feasible. Perhaps a central organization could be set up to facilitate and coordinate such research.

Because there are after all only 23 pairs of chromosomes in man, the time has come to start routine searching for linkage between continuous variables and bloodgroups or other single gene markers as advocated by Thoday. To make this more practical there may also have to be a central facility which would provide serology laboratory services by airmail and computer facilities. The basic principles have been worked out and several computer programs for this purpose are now available from Elston.[1]

The method of co-twin control studies, which permits study of the influence of specific environment on a constant genotype, seems to have been completely abandoned. Even relatively small efforts, say with 10 to 15 pairs of identical twins, would be very informative. At best the twins would attend a special nursery or kindergarten in which, for example, one of each pair was given number games and the other pre-reading games. Vandenberg explored this approach during one summer in Louisville and found it quite feasible.

WITHIN AND BETWEEN ETHNIC GROUP COMPARISONS:

For theoretical reasons we need to study cognition crossculturally, if we are to arrive at biologically relevant generalizations about the species.

It is my considered opinion that attempts to estimate heritabilities in American Negroes, Mexican Americans or American Indians will be quite informative about heredity-environment interactions and will tend to show that heritability estimates on whites cannot serve as the basis for inferences about racial differences in ability. While this point should be obvious, it apparently is not widely understood and may need many more experimental demonstrations than the one small study of Vandenberg (1970).

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[1] More information may be obtained from R.C.Elston, Department of Statistics, University of North Carolina

If at this time it seems more expedient for political reasons not to do such studies on Negroes in the continental United States, they could be done, perhaps also at less expense, on other ethnic groups in Hawaii; or in Puerto Rico or Alaska; or even in Brazil.

There has been some talk about assignment of an index of white gene admixture to each of a number of Negroes in a study, using gene frequencies of ancestral African and white groups to arrive at the probability that a given allele is of white ancestry and weighting a number of these alleles to obtain for each person a total value (in the nature of a proportion of white genes in the total genome). This value can then be correlated with ability test scores. While there are at the moment too few well established "African" frequencies for genetic markers to use this method (Reed,1969), it will eventually be possible to do so.

Again I would not expect such a study to provide simple results which would give comfort to either racists or over-eager equalitarians. If skin color and socioeconomic status were also measured, I would predict large interaction and covariance effects that may well outweigh additive genetic variance.

If such a bet came off we would have the best scientific argument for use by Equal Opportunity agencies that social intervention needs to be tailored to the specific groups with which one is working.

INTEGRATION OF BEHAVIOR GENETICS, BIOCHEMISTRY AND PHYSIOLOGY:

There is a good deal of research on animals in which techniques from biochemistry and/or physiology are combined with the methods of behavior genetics. However we are still lacking in convincing demonstrations of the fruitfulness of this combination in studies of man.

There have been many biochemical studies of schizophrenia particularly, but so far these have not been productive (Kety 1960, Rosenthal & Kety 1968). In part this may be due to a reliance on psychiatric diagnosis which may not only be inaccurate on occasion, but which could even be basically useless. The latter would be the case if there are several diseases with different modes of transmission but with somewhat similar behavioral effects. I, for one, do not see how one should proceed if one suspects that this is true. Nevertheless this area continues to hold enormous promise for the eventual understanding of how genes influence behavior. After all we often learn more about mechanisms and pathways from malfunctions than when everything works normally.

More promising than psychoses may be drug addiction, alcoholism and reaction to medical drugs. Psychopharmacogenetics may be an apt name for this research area.

MOST LIKELY FUTURE RESEARCH:

It is rather a safe bet to predict that there will be many more twin studies reporting on all kinds of variables. Such studies will in general not add much to our fundamental understanding, unless by chance or exceptional brillance the authors discover some variable which is primarily controlled by a single gene or which demonstrate at least considerable bimodality. Even then, pedigree studies will be needed to prove the Mendelian nature of the trait. To be of any use at all, future twin studies should at least include a sufficient number of ability, personality or perceptual variables to permit a meaningful multivariate analysis, so that a contribution can be made to the unresolved question whether or not there is an important general hereditary component or whether there are a number of equally important independent hereditary components in cognition. If the latter is true, such studies can also begin to explore the precise nature of these components, both at the phenotypic and at the genotypic level.

It is a discouraging thought that, in a way, much of the research represented by ability factor analyses will have to be repeated, with behavior genetic methods such as parent-offspring and twin studies.

Besides twin studies there will undoubtedly be new parent-offspring studies. Because earlier studies did not use measures of special or "primary" mental abilities, one may hope that future parent-offspring studies will use such tests. In that case they can also contribute to the multivariate problem mentioned above.

A very worthwhile contribution can be made by combining the twin study method with the parent-offspring method. Elston & Gottesman (1968) have provided a method for obtaining refined heritability estimates from such data.

Without additional effort such studies can also provide data for a study of assortative mating. There is no information about assortative mating for more modern, narrower and precise conceptions of special or "primary" abilities. Incidental to such work it would be interesting to know how several of these abilities are distributed in both sexes at various (middle) ages. Other than in one study from Holland, there is no such data. Even the distributions of these abilities in different socioeconomic classes are poorly studied (Verhage,1964).

In all the preceding and following remarks it should be noted that two parallel studies in rather different settings (or even different countries) would provide much more than twice the information. Perhaps it could be suggested to UNESCO that it would be worthwhile to organize multi-national studies of twins or of parents and their children. Such studies could provide much information about the effect of different environments on heritabilities.

The third and final safe bet is that there will be many more studies of the psychological concommittants of diagnosed genetic anomalies, both single gene substitutions and aneuploidies. While these will be interesting in themselves, use of a common set of psychological variables that will permit comparisons across studies is to be recommended. In an appendix at the end of this report an effort will be made to suggest some variables that would be useful common reference points.

NEEDED ANCILLARY RESEARCH:

We now come to some less central problem areas in which progress is necessary if we are to avoid much inconclusive research with poor methods. As in all sciences, improvement in techniques should not be seen as merely tedious "development rather than research" oriented efforts. Human behavior genetics is not unique in having to rely on the available psychological tests. Unfortunately we seem to be going through a period in which work on such "applied" problems is regarded as second rate, hardly worth the efforts of ambitious scientists. It may be time to call a halt to the research dependent on poorly developed, ad hoc measuring techniques. The hope for quick solutions by instruments created for a single study is often accompanied by a rather contemptuous attitude toward the somewhat less glamorous efforts of improving existing tests. Factor analysis has been one very potent technique in such efforts. Unfortunately it has rarely used outside criteria. While conventional factor analysis continues to clarify the relationship between the many existing ability measures, many questions remain unresolved, partly because of its reliance on group administered tests. A few examples will suffice to amplify this point.

1. We still do not understand well the processes required in the performance on the subtests of the three Wechsler intelligence tests although the studies by Cohen (1957,1959) and by Saunders (1959) have given us some broad outlines. More studies are needed such as the one by Davis (1956) in which the Wechsler subtests as well as a carefully chosen set of factorially relatively "pure" tests are administered.

2. We have only glimmerings of understanding about the relationship of

success on the Piagetian tasks and their associated stages to conventional psychometric measures. Again, some beginnings have been made but much more work is needed, if possible on substantially larger samples without sacrificing the "clinical" quality of such investigations.

3. Research on the development of language will someday have to be integrated with the measurement of intelligence in young children.

4. The relation between individual performance on various types of learning tasks and psychometric ability measures has received little attention although a few promising studies exist.

The same problems exist in even more marked form in the area of personality, where there exists even less of a consensus about the relative merits of different approaches. The behavior geneticist is confronted with a large number of personality questionnaires and other tests, each supported by an increasing bibliography and advocated by devoted users. With the exception of a recent study by Sells (1970), there has not been any major attempt to relate the various questionnaires to one another, nor have there been systematic studies of test-retest correlations and attempts to understand lack of repeat reliability in terms of individual dynamic processes affecting responses to such tests on different occasions.

Cattell's efforts to develop "performance" measures of personality, just as similar work by Thurstone at an earlier date, have been largely ignored, nor has the possibility been explored that some of Guilford's very many ability measures may to some degree measure personality.

One promising way to make progress in the test construction area has been proposed by Loehlin (1965) in his analysis of test items which showed high concordance for MZ twins but not for DZ. Tests specifically tailored for behavior genetics studies by this method or similar ones may well prove to be useful for other types of research as well.

The flip side, as disk jockeys say, of genetics, is environmental influences. The assessment of environmental factors influencing cognitive factors is a very difficult task that has perhaps too often been left to sociologists, because it is not easily brought under experimental control. The result is that there are many vague general statements but little hard knowledge. Perhaps the broad outlines of how such an assessment should proceed can be indicated but little progress in refining these ideas has been made since Barbara Burks' 1928 paper, except for the very fine-grained analyses by scientists studying infantile perception of patterned versus non-patterned stimuli, of the child's language environment, of mother-child interactions, or the more "impressionistic" formulations by cultural anthropologists.

Considering past efforts, some requirements can be specified.

Environmental assessment needs to take into account several levels or types of information.

1. Socioeconomic status. Warner's triplet: occupation, education and type of home still provides a good measure and up to date revisions are available (Reiss,1961).

2. Size and composition of the family, plus ordinal position of a given child. These easily obtained data may not add much over and above that obtained from the first category except for within family variance.

3. Psychological atmosphere in home:

   a. As indicated by more objective items such as number of books, types of magazines, membership of parents in clubs or other organizations, hobbies of child and parents.

   b. More "psychological" attributes that are more difficult to assess: Parental attitudes, expectations for the child's career and type of disciplinary control. Parent questionnaires may give mainly their perception of the currently fashionable child rearing practice.

Some shrewd interviewers can do fairly well in getting below this surface impression. Some teachers may also be able to provide useful data.

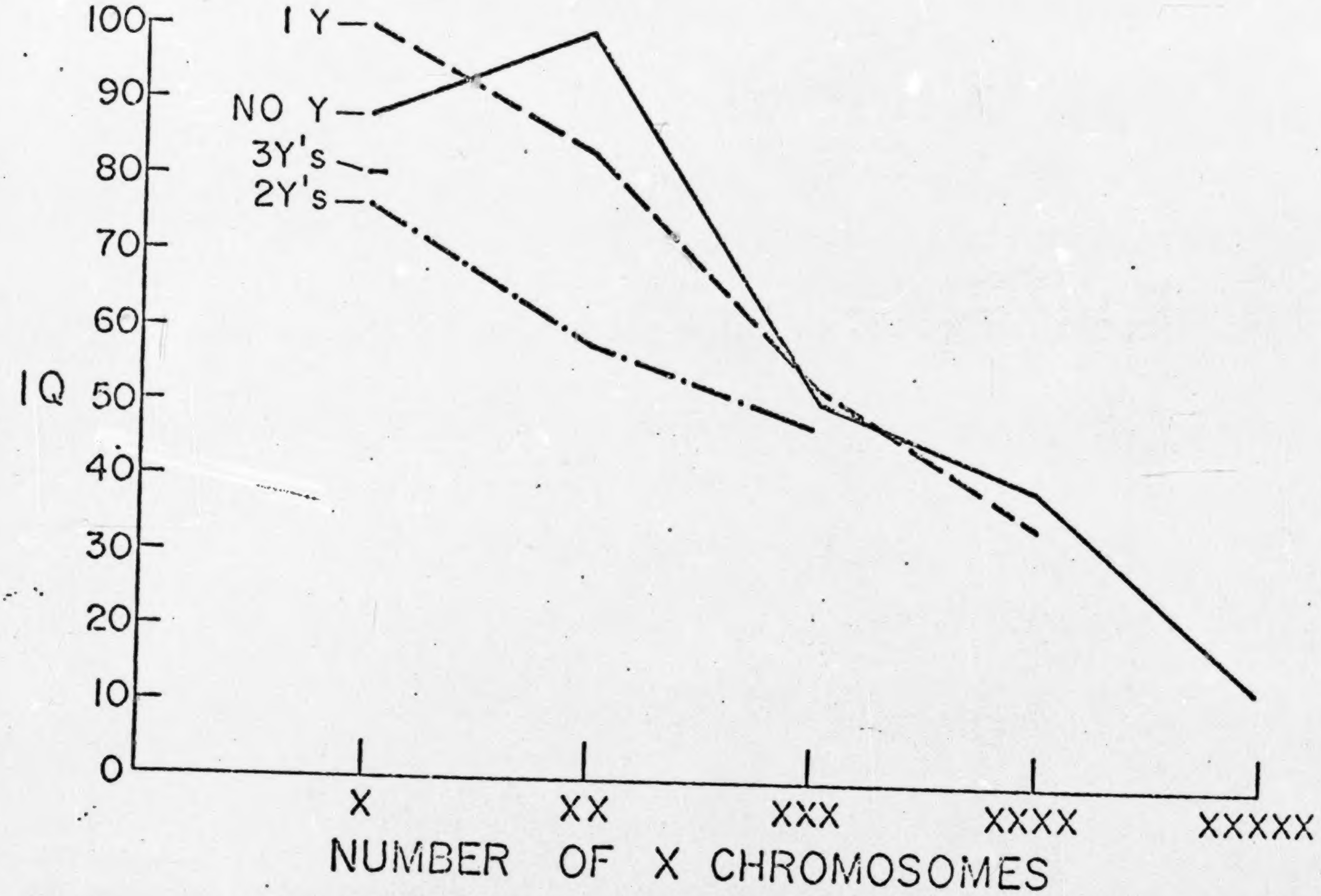
NEED FOR "BASIC" THEORETICAL FORMULATION:

On a much more theoretical level, we are lacking well worked out approaches to the structure of populations with respect to ability measures. While there are some large bodies of data that are relevant, most of these were collected without benefit of modern ideas about gene pools with restrictions on gene flow between these pools. We know next to nothing about factors controlling social mobility except for some highly visible, uniquely human attributes such as outstanding school grades, great beauty or social charm and exceptional athletic or artistic gifts. Even these we know about mainly on an anecdotal or common sense basis. Purely theoretical work and computer modeling may help to advance our understanding of the very complex multidimensional processes governing the changing distributions of genes influencing psychological variables. It should be understood that few individuals are capable of undertaking worthwhile work in this area. An evolutionary perspective would have to be formulated in which the personal motives of many individuals who mate and reproduce and the often unintentional but sometimes serious ecological consequences of industrialization and continued expansion of human populations are interacting in subtle ways.

Such theories may soon be needed to justify decisions related to curtailment of reproduction or economic penalties for producing retarded children, since various organizations are urging legal measures to curb the population explosion.

FIGURE 1

MEAN IQ OF INDIVIDUALS WITH ABNORMAL NUMBERS OF SEXCHROMOSOMES (MOOR 1967)



APPENDIX 1.

SUGGESTIONS FOR "CORE" DATA TO BE COLLECTED IN COOPERATIVE STUDIES.

Karyotypes preferably with the newer techniques of Caspersson et al.(1971), or of Drets & Shaw (1971), or if this is not possible, determination of Barr bodies.

Birthweight and data on subsequent physical growth to be compared to standards.

Height of father, mother and sibs.

Parental ages at birth of proband and ages of other children.

Fingerprints and palm prints.

General intelligence: IQ (Wechsler if possible, otherwise Stanford Binet) plus similar measures of both parents. If no individual testing is possible, children of at least low average ability, who are in school, may have been tested there with a group test.

Social competence: Vineland social maturity scale.

Patterning of abilities: Wechsler subtests, better yet, scores on special tests of separate abilities such as PMA, Pacific Multifactor tests (Meyers,et al. 1962,1964), or some European test battery.

Photos of proband repeated at following visits. (perhaps somatotype).

Sexual identity or gender role questionnaire and when techniques become available quantitative sex hormone assay.

EEG - especially Kappa-waves.

Teacher ratings of aggressiveness, popularity, outgoingness or sociability ("compared to all the youngsters you have known, how do you think x rates?")

If proband is capable of it, a personality questionnaire such as the one by Porter and Cattell (1968).

If more extensive ability testing is desired, the E.T.S. kit of reference tests should be consulted (French,1951, French,et al. 1963).

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